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Proposed Re-evaluation Decision PRVD2017-18

Permethrin and Its Associated End-use Products

Consultation Document

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Overview

In Canada, pesticides are regulated under the *Pest Control Products Act*, administered by Health Canada's Pest Management Regulatory Agency (PMRA). All pesticides are registered (that is, approved) if a rigorous scientific assessment indicates that the health and environmental risks are acceptable and the products have value. The *Pest Control Products Act* also contains provisions for postmarket reviews of registered pesticides namely, re-evaluation and special reviews, to assess whether pesticides continue to meet Health Canada's health and environmental standards, and whether they can continue to be used in Canada.

As part of the decision making process, before making a final decision, the PMRA consults with the members of the public and other interested stakeholders on all proposed major decisions such as new registrations, re-evaluations and special reviews. The PMRA encourages the public and stakeholders to participate in the consultation process. The proposed decisions are made based on the information available at the time, and the PMRA will consider the comments and information received during consultation using a science-based approach before making a final decision. The final decision will be published on the Pesticides and Pest Management portion of the Canada.ca website, and it will include a summary of the comments received during the consultation and the PMRA's responses to the comments.

The registration status of products and conditions of use of pesticide products on the market are not impacted by proposed re-evaluation or special review decisions. This may be the case only when final decisions are made. However, at any point during the re-evaluation or special review of a pesticide, the *Pest Control Products Act* allows the PMRA to cancel or amend the registration of registered pest control products, if there are reasonable grounds to believe this is necessary to deal with a situation that endangers human health or safety or the environment.

Proposed Re-evaluation Decision for Permethrin

An evaluation of available scientific information has determined that under the proposed conditions of use, the human health and environmental risks estimated for permethrin meet current standards for most uses. As a requirement for the continued registration of permethrin, new risk-reduction measures are proposed for certain commercial-class end-use products registered in Canada. Additionally, the following uses are proposed for cancellation due to lack of data to assess their risks to human health:

- Use in mushroom houses
- Application using foggers and hand-held mist sprayers/blowers
- Application of domestic-class products using foggers, hand-held mist sprayers/blowers

Any additional data/information submitted during the consultation period to further refine the health risk assessment will be considered, and may or may not result in a change to this proposal.

This Proposed Re-evaluation Decision is a consultation document[1] that summarizes the science evaluation for permethrin and presents the reasons for the proposed re-evaluation decision.

This consultation document is presented in two parts. The Overview describes the regulatory process and key points of the evaluation, while the Science Evaluation provides detailed technical information on the assessment of permethrin.

The PMRA will accept written comments on this proposal up to 90 days from the date of publication of this document. Please forward all comments to Publications (please see contact information indicated on the cover page of this document).

What Does Health Canada Consider When Making a Re-evaluation Decision?

The PMRA's pesticide re-evaluation program considers potential risks, as well as value, of pesticide products to ensure they meet modern standards established to protect human health and the environment. Regulatory Directive DIR2016-04, *Management of Pesticides Re-evaluation Policy* presents the details of the current re-evaluation approach.

For more details on the information presented in this overview, please refer to the Science Evaluation of this consultation document.

What Is Permethrin?

Permethrin is a broad spectrum synthetic pyrethroid insecticide. It is registered for use on a wide range of crops including grains and oilseeds, legumes, horticultural crops, mushroom houses, ginseng, greenhouse and field grown ornamentals as well as tobacco. It is also registered for use on livestock, companion animals, forestry and woodlots, feedlots, termite treatment, pet premises, kennels, indoors and outdoors of homes, agricultural, commercial and institutional building, military clothing, mosquito netting and to soil around honey bee hives.

Permethrin end-use products are applied by farmers, farm workers and professional applicators using conventional aerial and ground equipment on crops and pour-ons, ear tags and in backrubbers for livestock. Permethrin end-use products are also applied by pest control operators using typical application equipment; and by the general public as spot on, treated collars, spray, powder and shampoo treatments on companion animals, and ready to use and pressurized spray cans for use indoors and outdoors. The PMRA plans to publish a document in the future providing a broader examination of spot-on products for pets.

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1 "Consultation statement" as required by subsection 28(2) of the *Pest Control Products Act*.

Health Considerations

Can Approved Uses of Permethrin Affect Human Health?

Additional risk-reduction measures are required on labels of products containing permethrin. Products containing permethrin are unlikely to affect your health when used according to the proposed label directions.

Exposure to permethrin may occur through the diet (food and drinking water), when handling and applying end-use products containing permethrin or when entering or contacting treated sites. When assessing health risks, two key factors are considered: the levels at which no health effects occur in animal testing and the levels to which people may be exposed. The dose levels used to assess risk are established to protect the most sensitive human population (that is, children and nursing mothers). As such, sex and gender are taken into account in the risk assessment. Only uses for which the exposure is well below the levels that cause no effects in animal testing are considered acceptable for registration.

Toxicology studies in laboratory animals describe potential health effects from varying levels of exposure to a chemical and identify the dose at which no effects are observed. The health effects noted in animals occur at doses more than 100-times higher (and often much higher) than levels to which humans are normally exposed when pesticide-containing products are used according to label directions.

In laboratory animals, technical grade active ingredient permethrin was highly acutely toxic via the oral route. It was of low acute toxicity by the dermal and inhalation routes, was minimally irritating to the eyes and mildly irritating to the skin. In one of two animal studies, permethrin demonstrated an allergic skin reaction. Transient itching, burning, tingling or numbness of the skin has been noted in humans exposed dermally to permethrin.

Registrant-supplied short- and long-term (lifetime) animal toxicity tests, as well as information from the published scientific literature were assessed for the potential of permethrin to cause neurotoxicity, immunotoxicity, chronic toxicity, cancer, reproductive and developmental toxicity, and various other effects. The most sensitive endpoints for risk assessment were effects on the nervous system, the liver and on body weight. Following extended dosing, benign lung tumors in mice and liver and thyroid tumors were seen in rats. There is evidence of sensitivity of the young when directly exposed to permethrin. The risk assessment protects against the effects of permethrin by ensuring that the level of human exposure is well below the lowest dose at which these effects occurred in animal tests.

Pesticide Residues in Food and Drinking Water

Dietary risks from food and drinking water are not of concern when products containing permethrin are used according to the proposed label directions.

Reference doses define levels to which an individual can be exposed over a single day (acute) or lifetime (chronic) and expect no adverse health effects. Generally, dietary exposure from food and water is acceptable if it is less than 100% of the acute reference dose or chronic reference

dose (acceptable daily intake or ADI). An acceptable daily intake is an estimate of the level of daily exposure to a pesticide residue that, over a lifetime, is believed to have no significant harmful effects. For the cancer assessment, a lifetime cancer risk that is less than one-in-a-million (1×10^{-6}) is generally considered an acceptable risk for the general population when exposure occurs through pesticide residues in/on food and drinking water, and to otherwise unintentionally exposed persons.

The dietary assessment for permethrin included the potential for exposure to permethrin residues in treated crops and animal commodities (including imports), and drinking water for the general population and different subpopulations, including children and women of reproductive age.

The acute, chronic and cancer dietary exposure estimates were based mostly on monitoring data and included experimental processing factors when available. Field trial data and maximum residue limits (MRLs) were also used for commodities where monitoring data were not available. In addition, for the chronic and cancer assessments, domestic/import statistics and percent crop treated information were used, where available. Estimated environmental concentrations (EECs) in drinking water were based on the modelling of permethrin residues in surface and ground water using the application rates for tomato, as this crop had the highest annual application rate across Canada.

The acute dietary exposure (from food and drinking water) estimates at the 95th percentile were at or below 16% of the acute reference dose for all subpopulations, with children 1-2 years old being the highest exposed subpopulation. The chronic non-cancer dietary exposure estimates to permethrin from food and drinking were below 2% of the acceptable daily intake for all subpopulations with infants (< 1 year old) being the highest exposed subpopulation. The dietary cancer assessment based on the current use pattern indicated that cancer dietary risk from exposure to permethrin may be of concern. However, when mitigation measures are considered for existing uses (in other words, five applications are proposed for use on tomato instead of the six applications stated on the current labels.), the cancer risk from food and drinking water exposure is estimated as being at the threshold of acceptability (1×10^{-6}) for the general population and thus, is not of concern.

The *Food and Drugs Act* prohibits the sale of adulterated food; that is, food containing a pesticide residue that exceeds the specified MRL. Pesticide MRLs are specified for *Food and Drugs Act* purposes through the evaluation of scientific data under the *Pest Control Products Act*. Each MRL value defines the maximum concentration as parts per million (ppm) of a pesticide allowed in or on certain foods when a pesticide is used according to label directions, and serves as a food safety standard. The Canadian Food Inspection Agency is responsible for monitoring the Canadian food supply for pesticide residues and the determination of compliance with MRLs specified by Health Canada.

Canadian MRLs for permethrin are currently specified for a wide range of commodities. Residues in all other agricultural commodities, including those approved for treatment in Canada but without a specific MRL, are regulated under Subsection B.15.002(1) of the Food and Drugs Regulations, which requires that residues do not exceed 0.1 ppm. A complete list of MRLs specified in Canada can be found on the PMRA's MRL Database, an online query application

that allows users to search for specified MRLs, regulated under the *Pest Control Products Act*, for pesticides or food commodities (http://pr-rp.hc-sc.gc.ca/mrl-lrm/index-eng.php).

Risks in Residential and Other Non-Occupational Environments from Permethrin

Risks to residential handlers are not of concern for most uses when permethrin is used according to the proposed label directions.

Residential exposure may occur from the application of domestic class products containing permethrin to residential lawns, gardens and trees, outdoor and indoor environments, and pets. These products can be applied by manually pressurized handwand, aerosol can, trigger spray bottles, and spot-on treatments (pets).

For all domestic class products, no risks of concern were identified for most scenarios of individuals applying permethrin. However, no data were available to assess exposure when using hand-held mist sprayers/blowers and foggers. Therefore, products that need to be applied using this equipment are proposed for cancellation. For other products that could be applied using this equipment, label directions are proposed prohibiting application with these types of equipment.

Non-occupational risks for residential postapplication exposure are not of concern for most uses when permethrin is used according to the proposed label directions.

Residential postapplication exposure may occur while performing activities in treated areas. Treated areas include those treated by residential handlers as well as residential areas treated by commercial applicators. Exposure would be predominantly by dermal and inhalation routes. Incidental oral exposure may also occur for young children playing in treated areas or in contact with treated pets.

For most residential postapplication activities no risks of concern were identified for any population, provided mitigation measures, such as lower application rates, are implemented. Risks of concern were identified for postapplication exposure after indoor solid fogger application and indoor broadcast application. These uses are proposed for cancellation as mitigation is not considered to be feasible. For incidental oral exposure, no risks of concern were identified for young children.

Incidental oral, dermal and inhalation scenarios, when applicable, were aggregated with background (chronic) dietary exposure (food and drinking water). The aggregate cancer risk was determined using biomonitoring data. The calculated cancer risk was slightly above the threshold of acceptability. However, when considering the proposed mitigation measures, the conservatisms and uncertainties associated with use of biological monitoring data, and the degree to which the cancer threshold was exceeded, the aggregate cancer risk was considered to be not of concern.

Occupational Risks from Permethrin

Occupational risks to handlers are not of concern for most uses when permethrin is used according to the proposed label directions.

Occupational handler risk assessments consider exposure to workers applying permethrin in agricultural, commercial, and residential sites, and to military clothing. No risks of concern were identified for most of the commercial applicator scenarios in agricultural, commercial, and residential sites and for military clothing using baseline personal protective equipment. As such, no mitigation measures are required for these scenarios. Mitigation measures, such as additional personal protective equipment, are proposed for applicators using mechanically pressurized handgun and airblast equipment. No data were available to assess exposure when using foggers and hand-held mist blowers. Label statements are proposed to prohibit application using these types of equipment.

Risks to commercial applicators using spot-on products on pets were assumed to be similar to or less than residential application risks for this same use scenario. No risks of concern were identified for residential application of spot-on treatments on pets.

No risks of concern were identified for the industrial treatment of wood using a linear system.

Occupational risks for postapplication workers are not of concern for most uses when permethrin is used according to the proposed label directions.

Occupational postapplication risk assessments consider exposures to workers entering treated agricultural and residential sites, and military personnel wearing treated uniforms. Based on the current use pattern for permethrin, risks to workers performing agricultural activities, such as thinning, pruning and harvesting of all crops, meet current standards and are not of concern for most scenarios, provided mitigation measures such as restricted-entry intervals are implemented. The restricted-entry intervals required to mitigate agricultural postapplication risk range from 0.5–15 days. No risks of concern were identified for military personnel wearing treated military uniforms.

Postapplication exposure following livestock treatment is expected to be minimal. Postapplication exposure in feedlots is expected to be low due to the lack of postapplication activities where workers may come in contact with treated surfaces.

There is potential for postapplication exposure in mushroom houses. Currently, there are no data to estimate exposure to workers entering treated mushroom houses. No data are available to also determine transferable residues of permethrin from treated surfaces, or air concentrations after application. Therefore, a postapplication exposure assessment could not be conducted for mushroom houses. Thus the use is proposed for cancellation.

Risks for postapplication workers in residential areas were assumed to be similar to or less than residential postapplication risks for this same use scenario. No risks of concern were identified for residential postapplication scenarios provided that measures required to mitigate residential postapplication risk are implemented.

Environmental Considerations

What Happens When Permethrin Is Introduced into the Environment?

Permethrin is not expected to pose a risk of concern when used according to proposed label directions. Permethrin may pose a risk to aquatic organisms, bees, beneficial insects and birds; therefore, preventative measures to reduce risk to these organisms are proposed. When proposed label directions are followed, the risks are considered acceptable.

When permethrin is released into the environment, it can enter soil and surface water where it can persist under certain conditions. In soil, permethrin binds strongly to soil particles, making it unlikely to move downward in the soil and reach groundwater. In aquatic environments, permethrin rapidly moves out of water and into sediment where it can persist. Permethrin is unlikely to persist in air or move in air to remote locations such as the arctic. Permethrin is not likely to accumulate to levels of concern in the tissues of organisms, such as fish.

In terrestrial environments, permethrin can pose a potential risk to bees and other pollinators, as well as beneficial insects and birds if they are exposed to high enough levels of this pesticide. The risk to bees can be reduced by restricting or prohibiting the application of permethrin during the crop blooming period. The risk to beneficial insects living in habitats adjacent to the application site may be reduced by minimizing spray drift. Precautionary label statements are proposed on permethrin product labels to inform users of the potential hazard to bees, beneficial insects and birds and indicate the risk reduction measures that must be followed.

In aquatic environments, water modelling indicates that permethrin may be found at concentrations that pose risks of concern to aquatic invertebrates, fish and amphibians. Canadian water monitoring information confirms that, although rarely detected, permethrin can be found in aquatic environments at concentrations that would be expected to pose risks to aquatic invertebrates, fish and amphibians. Spray buffer zones are therefore proposed to protect aquatic organisms from spray drift. To reduce the risks of permethrin being carried in runoff to aquatic environments, in addition to precautionary label statements, a mandatory requirement for the construction and maintenance of a 10 m vegetative filter strip between the area of application and waterbodies is proposed.

Value Considerations

What is the value of permethrin?

Permethrin has one of the broadest use patterns for the synthetic pyrethroids. It contributes to resistance management by helping delay the development of resistance when used in rotation with other insecticides with different modes of action. Permethrin has a role in an integrated pest management approach for pests in structural sites. It is used by professional pest control applicators in residential settings to treat for bedbugs and fleas. Domestic products containing permethrin are registered for use against a broad spectrum of pests, such as ants, cockroaches and fleas.

These products are of benefit for homeowner use along with other control methods, such as prevention and non-chemical treatments, in the management of pests in and around the home. Various types of domestic permethrin products are used to control fleas, ticks, mosquitoes and lice on dogs..

Proposed Measures to Minimize Risk

Labels of registered pesticide products include specific instructions for use. Directions include risk-reduction measures to protect human health and the environment. These directions must be followed by law. As a result of the re-evaluation of permethrin, the PMRA is proposing the following risk-reduction measures for product labels:

Human Health

- Cancellation of use in mushroom houses due to lack of data to assess this use.
- Cancellation of certain application types (fogger, handheld mist blower/airblast) due to lack of data to assess these application types, and cancellation of other application types (indoor broadcast, indoor solid fogger) to address health risks of concern.
- A 60-day plant-back interval for all non-registered agricultural food/feed crops.
- For agricultural uses a restricted-entry interval of 12 hours for most crops and activities, and a longer interval for certain crops and activities (for example, hand-harvesting of grapes and sweet corn).
- The number of applications on tomato per year to be reduced from six to five applications.
- Additional personal protective equipment requirements for all agricultural product labels as well as all mechanically pressurized handgun applications, mosquito abatement truck mounted mist blower and airblast applications, and wood treatment in enclosed linear systems.
- The rate for application to lawns and turf is proposed to be limited to the lower registered rate of 0.123 g a.i./m^2.
- Additional label statements to minimize human exposure from spray drift or spray residues for domestic and commercial products used in residential areas.

Environment

- Environmental hazard statements for bees, beneficial insects, birds and aquatic organisms.
- To reduce risk to pollinators, application is to be restricted or prohibited during the crop blooming period.
- Label directions to minimize spray drift in order to reduce risk to beneficial insects living in habitats adjacent to the application site.
- Spray buffer zones for non-target aquatic habitats.
- Precautionary statements for sites with characteristics that may be conducive to runoff and when heavy rain is forecasted, in order to reduce the potential for runoff of permethrin to adjacent aquatic habitats.
- A mandatory vegetative filter strip between the treatment area and the edge of a water body to reduce run-off of permethrin to aquatic environments.

What Additional Scientific Information Is Requested?

No additional data are required.

Next Steps

During the consultation period, registrants and stakeholder organizations may submit further data that could be used to refine risk assessments (exposure or use information), which could result in revised risk-reduction measures. Stakeholders who are planning to provide information of this type are advised to contact the PMRA early in the consultation period, for advice on studies or information that could be submitted to help refine the relevant risk assessments.

Before making a final re-evaluation decision on permethrin, the PMRA will consider all comments received from the public in response to this consultation document. The PMRA will then publish a Re-evaluation Decision[2] that will include the decision, the reasons for it, a summary of comments received on the proposed decision and the PMRA's response to these comments.

2 "Decision statement" as required by subsection 28(5) of the *Pest Control Products Act*.

Science Evaluation

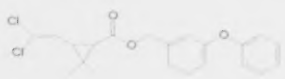
1.0 Introduction

Permethrin is a broad spectrum synthetic pyrethroid with stomach and contact action. It is a non-systemic insecticide that acts on insect nervous systems.

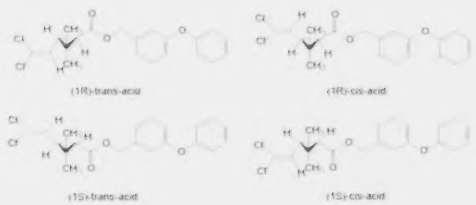
Following the re-evaluation announcement for permethrin, the registrant of the technical grade active ingredient and primary data provider in Canada indicated continued support for all registered label uses. All current uses were therefore considered in this re-evaluation. The purpose of this re-evaluation is to review existing information on permethrin and its currently registered technical, commercial and domestic class end-use products, to ensure that risk assessments meet current standards.

2.0 The Technical Grade Active Ingredient, Its Properties and Uses

2.1 Identity of the Technical Grade Active Ingredient.

Common name		Permethrin
Function		Insecticide
Chemical Family		Pyrethroid
Chemical name		
1	**International Union of Pure and Applied Chemistry (IUPAC)**	3-phenoxybenzyl (1*RS*,3*RS*;1*RS*,3*SR*)-3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropanecarboxylate or 3-phenoxybenzyl (1*RS*)-*cis-trans*-3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropanecarboxylate
2	**Chemical Abstracts Service (CAS)**	(3-phenoxyphenyl)methyl 3-(2,2-dichloroethenyl)-2,2-dimethylcyclopropanecarboxylate
CAS Registry Number		52645-53-1
Molecular Formula		$C_{21}H_{20}Cl_2O_3$
Structural Formula		

Four isomers:



Molecular Weight 391.3

Registration Number	Purity of the Technical Grade Active Ingredient
18059	96%
18090	95.00%
20991	95.0%
25459	96.0%
28524	96.0%
28932	98.2%

2.1 Physical and Chemical Properties of the Technical Grade Active Ingredient

Property	Result
Vapour pressure at 25°C	0.0029 mPa
Ultraviolet (UV) / visible spectrum	λ_{max} = 214 nm (neutral pH, in methanol) λ_{max} = 215 nm (pH 1.6, in methanol) λ_{max} = 227 nm (pH 13.98, in methanol) Does not absorb at $\lambda > 350$ nm
Solubility in water (20-25°C)	0.006 mg/L
n-Octanol/water partition coefficient	Log K_{ow} = 6.1
Dissociation constant	Not applicable

2.3 Description of Registered Permethrin Uses

As of 1 March 2017, six technical grade active ingredient products, 14 manufacturing products, 44 commercial products and 337 domestic products containing permethrin were registered in Canada. Formulations include emulsifiable concentrate, liquids, pressurized gas, solids, solutions, suspensions and eartags for cattle. Permethrin labels can be accessed through the PMRA's label transcription service.[3]

All uses supported by the registrants at the time of re-evaluation initiation were considered in the risk assessments of permethrin. Maximum application rates were used in the risk assessment. When application rates were not available from Canadian labels, the maximum application rates from the United States (US) labels were used instead. When application rates were not provided on Canadian or American labels, it was calculated based on product and use information. The United States Environmental Protection Agency (USEPA) has generated standard default assumptions for developing residential exposure assessments for both applicator and postapplication exposures. These assumptions were used in the absence of, or as a supplement to, chemical- and/or site-specific data, as outlined in the Standard Operating Procedures (SOP) for Residential Pesticide Exposure Assessments (USEPA, 2012).

3.0 Impact on Human and Animal Health

3.1 Toxicology Summary

Technical permethrin is a Type I synthetic pyrethroid insecticide which lacks a cyano group at the α carbon position of the alcohol moiety. The primary target of type 1 pyrethroids is the nervous system through interference with axonal sodium channels in the nerve membrane. This interference with sodium channels leads to the repetitive firing of affected nerves, generating signs of neurotoxicity which could include hyper-excitability, muscle spasms, tremors, paralysis and death.

A detailed review of the toxicological database for permethrin was conducted. The majority of the available toxicity studies were conducted in the 1970s. Considered individually, some of these studies do not meet the current standards for testing, although they were considered acceptable at the time of their initial evaluation. Some of the studies were conducted with test compounds that were not adequately identified and characterized chemically, and the dose levels were not verified by adequate dietary analyses for homogeneity, stability and/or concentration of the test material. The extensive database was supplemented by numerous publications from the scientific literature; some of these studies also lacked characterization of the isomeric ratio. Taken together, the data from these studies, in addition to information from the published literature, provide sufficient information for risk assessment purposes.

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[3] PMRA's label transcription service is available online here: http://pr-rp.hc-sc.gc.ca/ls-re/index-eng.php. Pesticide labels can also be accessed on a mobile device using the pesticide label app available here: https://www.canada.ca/en/health-canada/services/consumer-product-safety/pesticides-pest-management/registrants-applicants/tools/pesticide-label-search.html.

Permethrin is a racemic mixture comprised of cis- and trans- isomers. In Canada, the cis:trans ratio of registered technical permethrin is approximately 40:60. Toxicology data conducted with this representative isomeric content were considered foremost in the review; however, studies with differing isomeric ratios have also been considered. Reasons for considering data conducted with non-representative isomeric content include the potential for permethrin of differing isomeric content to be present on imported crops and to provide support in cases where isomeric-relevant studies may have limitations.

Permethrin, radiolabelled with ^{14}C, was rapidly absorbed, distributed and excreted as metabolites in the urine and feces of orally-exposed rats and dogs. After oral administration, permethrin was absorbed through the intestine and transported via the blood to various tissues including the liver, lungs, kidneys and fat. Detectable residues were also noted in the muscle and brain. Peak levels of radioactivity were reached in most tissues within 4 hours post-dosing, declining rapidly, except in fatty tissues, within 24 hours. Most of the administered dose was eliminated within 48 hours. Administration of a single low oral dose to rats resulted in elimination via the urine (50-62%) and feces (36-49%); a single high dose increased the fecal excretion to 71-76%. In dogs, urinary excretion accounted for 31-43% and fecal excretion accounted for 46-56% with a single low oral dose. The half-life of permethrin in rat adipose tissue was approximately 7-18 days and close to 7 weeks was required for the complete elimination of radiolabel from adipose tissue in the rat following the termination of repeated dosing. With repeated oral dosing, dogs showed higher retention of permethrin in fat than rats.

In both rats and dogs, greater cis- isomer content in the adipose tissue following oral administration of permethrin indicated that the trans- isomer was more readily metabolized. This was further supported by the pattern of higher urinary elimination (79-82%) when trans-permethrin was orally administered to rats compared to that associated with cis-permethrin administration (52-54%). A similar excretion pattern was noted in dogs with the cis- and trans-isomer.

Metabolism of permethrin in rats and dogs was extensive, with no significant difference noted between males and females. The major metabolic pathway of permethrin in the rat involved ester cleavage followed by hydroxylation and conjugation of the cleaved metabolites with either glucuronic acid, glycine or sulphate. The major urinary metabolite of ^{14}C-acid permethrin was dichlorovinyl acid glucuronide, while minor metabolites in the urine were free cis- or trans-dichlorovinyl acid. The major urinary metabolites of ^{14}C-alcohol permethrin were 4'-hydroxyphenoxy-benzoic acid sulfate, phenoxybenzoic acid in the free form and its glucuronic acid and glycine conjugates. The principal fecal metabolites with ^{14}C-acid cis-permethrin were unchanged permethrin and hydroxylated metabolites retaining the ester linkage. Four hydroxylated ester derivatives of permethrin were identified in the feces of the rats given ^{14}C alcohol cis-permethrin along with unchanged parent. These metabolites were not present in the feces of rats given ^{14}C-alcohol trans-permethrin, in which the identified metabolites were phenoxybenzyl alcohol, phenoxybenzoic acid and unchanged parent. Metabolism of parent material is rapid and extensive, with only between 3 and 6% of the administered dose being recovered as unmetabolized permethrin in the feces.

The acute toxicity of permethrin varied significantly and depended on the cis:trans isomer ratio and vehicle. Corn oil was the predominant vehicle used in the toxicology studies due to its suitability for the lipid soluble properties of permethrin. In rats, the acute oral toxicity ranged from low toxicity for permethrin with lower cis-content to high toxicity for permethrin of representative and/or higher cis-content. Signs of toxicity included urinary incontinence, dehydration, piloerection, hypersensitivity, upward curvature of the spine, tremors, hyperthermia and irregular or increased breathing. When compared to adult rats, rat pups were more sensitive to the lethal effects of permethrin, with neonate and weanling pups demonstrating the lowest median lethal dose. There was little difference between the sexes with respect to acute toxicity.

In mice, the acute oral toxicity ranged from slight to moderate for permethrin with lower cis-content and from moderate to high for permethrin with representative and/or higher cis-content. Signs of toxicity in mice included hypersensitivity, tremors and ataxia. In guinea pigs and rabbits, the acute oral toxicity of permethrin of relevant isomeric content was low, with signs of lethargy, slight incoordination, piloerection, increased respiration, hunched posture, slight incoordination and tremors noted in rabbits only. Cats are particularly sensitive to the toxic effects of permethrin, in part, due to their deficiency in glucuronidase, required for the glucuronidation of permethrin, as well as the slow rate at which they hydrolyze permethrin.

Permethrin was of low acute toxicity to mice, rats and rabbits by the dermal route; signs of toxicity were limited to tremors in rats at high doses. Low acute toxicity was observed in rats exposed via the inhalation route; signs of toxicity included splayed gait, tremors, paw flicking, decreased reflexes and decreased activity.

Permethrin was minimally or mildly irritating to the eyes and skin of rabbits. In one of two guinea pig maximization studies, permethrin was shown to be a dermal sensitizer. In the second study, lower concentrations were utilized for both induction and challenge than in the positive study. Published studies that examined the skin of human subjects following the application of permethrin revealed mild erythema but little evidence of sensitization. More commonly reported in these human studies was the observation of transient paraesthesia.

In the short-term oral toxicity studies, there was a broad range of effect levels that varied based on the cis:trans isomer ratio of permethrin. Throughout the database, the primary target organs in mice, rats, rabbits and dogs were consistently the liver and the nervous system.

Effects on the liver following short-term oral exposure included hypertrophy of hepatocytes with associated biochemical and ultrastructural changes in rats and dogs and to a lesser extent in mice. In rats, the alterations in the liver were reversible on withdrawal of treatment following exposure to permethrin for 28 or 90 days. In rats and dogs orally exposed to permethrin, effects on the nervous system included hypersensitivity, piloerection, muscle twitching, impaired gait, involuntary limb movements, salivation, urinary incontinence, ataxia and tremors, with signs becoming more severe at higher oral doses. In some instances, the effects on the nervous system were reversible in those animals that survived exposure to the high dose levels. Rabbits demonstrated signs of neurotoxicity to a lesser degree than rats and dogs and these effects (mild hyperactivity and muscular fasciculations) were only noted at significantly higher dose levels. Other organs that were affected at higher dose levels in the repeat-dose oral toxicity studies included the kidney (mice, rats and rabbits), thymus (mice only), spleen (mice and rats), thyroid

(rats only) and the lungs (rats only). With chronic oral exposure in mice and rats, the effects were similar to those from short-term dosing and included the liver, nervous system, kidneys, lungs (mice only), thymus (rats only) and thyroid (rats only). There was no clear evidence that duration of repeated-dosing had an effect on toxicity.

In the 21-day dermal toxicity studies in rats and rabbits, no treatment-related effects were noted in animals at doses up to 500 mg/kg bw/day. Permethrin induced mild irritation at the application site in both rats and rabbits.

Consistent with oral studies, signs of neurotoxicity and hepatotoxicity were also noted in rats following inhalation exposure to permethrin for either fifteen days or thirteen weeks. In contrast, short-term inhalation toxicity studies in guinea pigs and dogs did not demonstrate any signs of neurotoxicity, even with permethrin of a higher cis-isomer content.

Dietary administration of permethrin resulted in an increased incidence of benign lung adenomas in female mice in two carcinogenicity studies and an equivocal increase in benign lung adenomas in a third study that was conducted with permethrin of lower cis-content (i.e. 25:75 cis:trans). A fourth non-guideline study conducted with very high doses of permethrin confirmed the treatment-related increased incidence of benign lung adenomas and demonstrated that the incidence was increased as early as 39 weeks. However, the lung adenomas did not occur any earlier in the treated animals than in the control groups. None of the studies showed a treatment-related increase in malignant lung tumours. Treatment-related lung adenomas have also been noted in studies conducted in female mice with cypermethrin, a structurally similar compound. Dietary exposure to permethrin also increased the incidence of hepatocellular adenomas in male mice in two carcinogenicity studies but not in a third study that was conducted with permethrin of a low cis-content. The incidence of hepatocellular adenomas was increased in female mice in two of the four available studies. A treatment-related progression to hepatocellular carcinomas was not observed in any of these studies. An increased incidence of thyroid adenomas was noted in female rats at the high-dose level in one of the two acceptable carcinogenicity studies conducted with permethrin. No increase in thyroid carcinomas was seen in these female rats. Based on the weight of evidence, it was determined that permethrin possesses tumorigenic potential; as such, a quantitative cancer risk assessment was undertaken.

A prospective cohort study of licensed pesticide applicators in Iowa and North Carolina, known as the Agricultural Health Study, examined the relationship between permethrin exposure and cancer incidence. No association between permethrin exposure and the incidence of all malignant neoplasms combined, or the incidence of melanoma, non-Hodgkins lymphoma, leukemia or cancers of the lung, bladder, colon, rectum or prostate was identified. An elevated risk for multiple myeloma among applicators in the highest tertile of lifetime exposure days or intensity-weighted lifetime exposure days was noted in comparison with non-exposed applicators; however, as noted by the study authors, due to the small number of exposed multiple myeloma cases, chance occurrence could not be ruled out.

Available in vivo studies, including dominant lethal, micronuclei and chromosome aberration assays demonstrated that permethrin was not genotoxic in these systems. Negative results were also obtained in a supplemental sex-linked recessive lethal test and host-mediated assay in mice. Permethrin was not genotoxic in a number of in vitro reverse mutation assays with *Salmonella*

typhimurium. Permethrin did not cause unscheduled DNA synthesis in primary rat hepatocytes. Although the submitted studies did not indicate genotoxic activity, two supplemental published studies suggested that permethrin had clastogenic activity (for example, micronuclei and induction of aberrations) in cultured human lymphocytes and Chinese hamster ovary cells, but only in the absence of metabolic activation at cytotoxic dose levels.

The reproductive toxicity of permethrin was investigated in three, three-generation toxicity studies in rats, of which one was deemed supplemental. In the supplemental study, there were no signs of reproductive, parental or offspring toxicity observed; however, the doses tested were low when compared to another study conducted with permethrin of lower cis-content. Although there was an increased incidence of eye effects (ocular hemorrhage and glaucoma) in the offspring, these were not considered treatment-related due to low incidence and lack of a dose-response.

In the three-generation reproductive toxicity study conducted with permethrin of representative isomeric content, clinical signs of neurotoxicity and effects on body weight gain and food consumption were noted in the parental animals at the same high dose level as effects on the offspring (whole body tremors). An increased incidence of buphthalmos (persistent pupillary membrane) was noted in F_{1b}, F_{2a}, F_{2b}, F_{3a} and F_{3b} weanlings; however, a dose-response relationship did not always exist and the incidence of buphthalmos was only slightly higher than the background incidence. It was possible that the buphthalmos reflected a spontaneous manifestation of a pre-existing genetic abnormality. For these reasons, definitive conclusions could not be drawn as to the relationship to permethrin treatment and the potential susceptibility of the pups.

In the rat gavage developmental toxicity study, signs of neurotoxicity, such as tremors and head flicking, in addition to decreased body weight gain and food consumption, were observed in maternal animals orally exposed to a high dose level. At the same dose level, the incidence of minor skeletal variations was increased and body weight was decreased in the fetuses, but there was no evidence of teratogenic potential at any dose level. In a gavage developmental toxicity study in rabbits, maternal animals were sacrificed moribund or found dead at relatively high dose levels. Treatment-related effects in the fetuses, including fetal loss and growth delay, occurred at doses exceeding the limit dose. In the available developmental toxicity studies, there was no evidence of increased susceptibility of rat or rabbit fetuses to permethrin.

Based on the Tier I weight-of-evidence evaluation of existing data by the USEPA Endocrine Disruptor Screening Program, permethrin has potential to interact with the androgen hormone system. In published studies, including three Hershberger assays, uterotrophic assays, cell proliferation assays, recombinant yeast screening assays, and a reporter gene assay, permethrin displayed weak anti-androgenic effects in male rats in vivo and in in vitro studies and even weaker estrogen-like effects in female rats in vivo and in in vitro studies.

In specialized published repeat-dose oral studies in male mice and rats, histopathological changes in the testes, abnormal sperm morphology decreased testicular and epidydimal sperm counts, decreased serum and testicular testosterone levels and decreased expression of androgen receptors and steroidigenic regulatory proteins were observed with oral administration of permethrin, or the cis- or trans-isomer of permethrin. Notwithstanding these observations, there

was a lack of functional or morphological changes in the testes noted throughout the permethrin database, except for decreased testicular weights in a supplemental two-year dietary study in mice. As the testicular function and morphology alterations in the published literature occur at doses above those selected for risk assessment, endpoints selected for risk assessment are protective of these effects.

The acute oral neurotoxicity guideline study was of questionable value due to a number of factors including the measurement of effects at a time-to-peak effect that was different than that which was established in other studies. Sufficient information to address acute neurotoxicity was available from six other acute studies in the published literature. These studies showed a consistent pattern of clinical signs of neurotoxicity, decreased motor activity and increased reactivity to stimuli. No evidence of neuropathology was observed in the acute studies. Similar clinical signs and behavioural responses were seen in repeat-dose oral neurotoxicity studies. At dose levels sufficient to produce clinical signs of intoxication in rats, permethrin caused swelling and degenerative changes (disintegration of axons, nodal demyelination, and disruption of the myelin sheath, degenerating nerve fragments and vacuolated Schwann cells) in sciatic nerves. Alterations in the sciatic nerves were also noted in a dermal neurotoxicity study conducted in rats exposed to very high dose levels of permethrin. Although no guideline developmental neurotoxicity study was available, an oral non-guideline study was available in the published literature which examined behavioural endpoints in the offspring of mice exposed to permethrin only prior to mating. Doses that produced clinical signs of neurotoxicity in the parents also produced behavioural changes in offspring.

Studies from the published literature indicate that age-dependent maturation of key metabolic processes may lead to increased susceptibility of the young to pyrethroid toxicity. Young animals have incomplete maturation of the enzyme systems that detoxify pyrethroids, particularly the carboxylesterases and cytochrome P450s. Consequently, pyrethroid concentrations in target tissues (for example, brain) may be higher in young animals than in adults given the same dose. In general, pyrethroid neurotoxicity is correlated to peak concentrations of the compound, with gavage dosing patterns resulting in greater internal doses compared to dietary administration. The pyrethroids are regarded as having a narrow window of time-to-peak-effect. The design of a developmental neurotoxicity study does not consider time-to-peak-effect and may miss the window of peak toxicity for the pyrethroids. The non-guideline DNT study that was available for permethrin was therefore considered of limited value in addressing residual concern for the young. A comparative oral gavage neurotoxicity study conducted in pups, weanlings and adults, which considers the time of peak effect, could address this uncertainty. In the interim, this uncertainty has been reflected in the form of a database uncertainty factor.

In a prospective cohort study in New York, no significant associations were noted between permethrin (either cis- or trans-) levels measured in the personal air samplers of women in the third trimester of pregnancy for 48 hours and the mental or motor development of their offspring at 36 months of age. Similarly, no significant associations were noted between permethrin (cis- or trans-) levels measured in maternal and/or umbilical cord plasma samples and the mental or motor development of the involved children at 36 months.

In hens, behavioural changes were observed following exposure to permethrin; however, no signs of treatment-related lesions of the central and peripheral nervous systems were noted. Permethrin did not induce delayed neurotoxicity in hens.

In acute dermal immunotoxicity studies in female mice, decreased thymic cellularity and weight were noted along with a reduced splenic T-cell proliferative response to a mitogen. In a repeat-dose dermal immunotoxicity study in mice, decreased thymic cellularity was recorded with different dosing regimes. A supplemental published immunotoxicity study was conducted with permethrin in female mice by the oral route. While this study lacked any details on the isomeric content of permethrin, the results of this study demonstrated an effect on the mixed lymphocyte response along with a decrease in the cytotoxic activity of T lymphocytes and natural killer cells at low dose levels. Given the immune responses noted in these studies, the lack of a guideline immunotoxicity study conducted by the oral route has been reflected in the form of a database uncertainty factor.

Results of the toxicology studies conducted on laboratory animals with permethrin, along with the toxicology endpoints for use in the human health risk assessment, are summarized in Appendix I, Tables 1 and 2.

3.1.1 *Pest Control Products Act* Hazard Characterization

For assessing risks from potential residues in food or from products used in or around homes or schools, the Pest Control Products Act requires the application of an additional 10-fold factor to threshold effects to take into account completeness of the data with respect to the exposure of, and toxicity to, infants and children, and potential pre- and postnatal toxicity. A different factor may be determined to be appropriate on the basis of reliable scientific data.

With respect to the completeness of the toxicity database as it pertains to the exposure of and toxicity to infants and children, extensive data were available for permethrin. The database contains the full complement of required studies including developmental toxicity studies in rats and rabbits and three multi-generation reproductive toxicity studies in rats, including a supplemental study. A non-guideline study examining behavioural endpoints in the offspring of mice exposed to permethrin only during pre-mating was available from the scientific literature. A guideline developmental neurotoxicity study was not available but as discussed previously, was not required for permethrin. Some comparative lethality data were available from the literature, which addressed age differences. A comparative neurotoxicity study in pups, weanling and adult animals was not available for permethrin.

With respect to potential prenatal and postnatal toxicity, there was no evidence of increased susceptibility of rat or rabbit fetuses to in-utero permethrin exposure in oral developmental toxicity studies. Fetal effects, including reduced weight, delayed ossification, minor variants and in the case of rabbits, fetal loss, occurred at maternally toxic levels. In the multi-generation reproductive toxicity studies in rats, there was no evidence of sensitivity of the young except for one study in which a slightly increased incidence of buphthalmos was noted in the offspring at a dose level that did not result in maternal toxicity.

As this effect could not be definitively linked to permethrin treatment, it was deemed insufficient for assessment of susceptibility of the young. Behavioural endpoints were affected in the offspring of mice exposed only during pre-mating to permethrin, but only at doses that caused signs of neurotoxicity in the parents.

Two studies from the literature addressed age-related sensitivity by comparing lethality of young and adult rats. Young rats were found to be at least 2-fold more sensitive than adults to the lethal effects of permethrin. It is known that young animals have incomplete maturation of enzyme systems which detoxify pyrethroids and, thus, may be more susceptible due to higher and prolonged brain concentrations, compared to adults. Due to the lack of a comparative oral neurotoxicity study, an adequate assessment of sensitivity of the young is currently not available and residual uncertainty remains concerning susceptibility of the young to potential neurotoxic effects. A 3-fold database uncertainty factor was applied for concerns regarding potential sensitivity of the young to neurotoxic effects and a 3-fold factor was applied for the lack of a guideline immunotoxicity study where relevant. Where both of these concerns were relevant to the scenario under consideration for risk assessment, only one 3-fold factor was applied. Since these concerns were addressed with a database uncertainty factor, the *Pest Control Products Act* factor was reduced to 1-fold for permethrin.

3.2 Dietary Exposure and Risk Assessment

In a dietary exposure assessment, PMRA determines how much pesticide residue in food, including residues in milk and meat, and in drinking water may be ingested with the daily diet. Exposure to permethrin from potentially treated imported foods is also included in the assessment. Dietary exposure assessments are age-specific and incorporate the different eating habits of the population at various stages of life (infants, children, adolescents, adults and seniors). For example, the assessments take into account differences in children's eating patterns, such as food preferences and the greater consumption of food relative to their body weight when compared to adults. Dietary risk is then determined by the combination of the exposure and the toxicity assessments. High toxicity may not indicate high risk if the exposure is low. Similarly, there may be risk from a pesticide with low toxicity if the exposure is high.

PMRA considers limiting use of a pesticide when dietary exposure exceeds 100% of the reference dose or the lifetime cancer risk estimate exceeds 1×10^{-6} (one-in-a-million). PMRA's Science Policy Note SPN2003-03, *Assessing Exposure from Pesticides, A User's Guide*, presents detailed acute, chronic and cancer risk assessment procedures.

Residue estimates used in the dietary risk assessment may be based conservatively (using upper bound estimates) on the maximum residue limits (MRL) or field trial data representing the residues that may remain on food after treatment at the maximum label rate. Surveillance data representative of the national food supply may also be used to derive a more accurate estimate of residues that may remain on food when it is purchased. These include the Canadian Food Inspection Agency's (CFIA) National Chemical Residue Monitoring Program and the United States Department of Agriculture's (USDA) Pesticide Data Program (PDP). Theoretical and experimental processing factors, as well as specific information regarding percent of crops treated may also be incorporated to the greatest extent possible.

In situations where the need to mitigate dietary exposure has been identified, the following options are considered. Dietary exposure from Canadian agricultural uses can be mitigated through changes in the use pattern. Revisions of the use pattern may include such actions as reducing the application rate or the number of seasonal applications, establishing longer pre-harvest intervals, and/or removing uses from the label. Imported commodities that have been treated also contribute to the dietary exposure and are routinely considered in the risk assessment. The mitigation of dietary exposure that may arise from treated imports is generally achieved through the amendment or specification of MRLs.

Sufficient information was available to adequately assess the dietary exposure and risk to permethrin. Acute, chronic and cancer dietary exposure and risk assessments for permethrin were conducted using the Dietary Exposure Evaluation Model - Food Commodity Intake Database™ (DEEM-FCID™; Version 4.02, 05-10-c) program which incorporates food consumption data from the National Health and Nutrition Examination Survey, What We Eat in America (NHANES/WWEIA) 2005-2010 available through the Centers for Disease Control and Prevention's National Center for Health Statistics. Further details on the consumption data are available in the Science Policy Note SPN2014-01: General Exposure Factor Inputs for Dietary, Occupational, and Residential Exposure Assessments. Acute and chronic dietary exposures were estimated from residues of permethrin in treated crops and animal commodities (including imports), and from drinking water.

The acute, chronic and cancer dietary exposure estimates for permethrin are considered to be highly refined (more precise) as monitoring residues from surveillance data, and experimental processing factors were used to the extent possible. In addition, for the chronic and cancer assessments, domestic production and import supply, as well as percent crop treated information were used, where available. For more information on dietary risk estimates or residue chemistry information used in the dietary assessment, see Appendices III and IV, respectively.

3.2.1 Determination of Acute Reference Dose (ARfD)

General Population (including pregnant women, infants and children):

To estimate acute dietary risk, the $BMDL_{20}$ (benchmark dose 95% lower confidence limit at the 20% effect level) of 22.95 mg/kg bw from an acute oral neurotoxicity study conducted with permethrin was selected, based on reduced motor activity in adult rats. Reduced motor activity was considered the critical endpoint, since it is a sensitive neurobehavioural endpoint which is relevant to pyrethroid toxicity and was derived by a relevant route and duration of exposure. The $BMDL_{20}$ was specifically selected based on the reported variability of motor activity in control rats in the literature. Given the reasons outlined in the *Pest Control Products Act* Hazard Characterization section, a 3-fold database uncertainty factor was applied for risk assessment purposes. Consequently, the *Pest Control Products Act* factor was reduced to 1-fold as discussed in the *Pest Control Products Act* Hazard Characterization section. Standard uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability were also applied, resulting in a composite assessment factor of 300.

$$\textbf{ARfD} = \frac{\textbf{22.95 mg/kg bw}}{\textbf{300}} = \textbf{0.08 mg/kg bw}$$

3.2.2 Acute Dietary Exposure and Risk Assessment

The acute dietary risk (from food and drinking water) was calculated considering the highest ingestion of permethrin that would be likely on any one day, and using food and drinking water consumption, and food and drinking water residue values. The expected intake of residues is compared to the ARfD, which is the dose at which an individual could be exposed on any given day and expect no adverse health effects. When the expected intake of residues is less than the ARfD, the acute dietary exposure is not of concern.

The acute refined deterministic dietary risk assessment was conducted for the general population and all subpopulations using available residue monitoring data from the CFIA and the USDA's PDP, and the highest anticipated residues from field trials or MRLs/tolerances for commodities for which no monitoring data were available. Residue adjustment factors were estimated from available field trials and metabolism data and used to account for residues of DCVA, MPBA and 3–PBA in commodities where these metabolites were identified as major residues. The PMRA's and US Environmental Protection Agency's (USEPA) policies were used for crop translations when necessary. In addition, experimental processing factors were used, where available. DEEM-FCID default processing factors were used when experimental processing factors were not available. Drinking water contribution to the exposure was accounted for by direct incorporation of the highest drinking water estimated environmental concentration (EEC) point estimate, obtained from water modelling (see Section 3.3), into the dietary exposure evaluation model (DEEM-FCID).

The acute dietary exposure (from food and drinking water) estimates for the general population and all subpopulations, at the 95th percentile, ranged from 9% of the ARfD (youth 13–19 years old) to 16% of the ARfD (children 1–2 years old), and are therefore not of concern.

3.2.3 Determination of Acceptable Daily Intake (ADI)

General Population (including pregnant women, infants and children):

To estimate dietary risk from repeated exposure, a NOAEL of 5.0 mg/kg bw/day was selected from the following co-critical oral toxicity studies: the 4-week behavioural mouse study with offspring assessment, a 90-day dog study, a 52-week dog study and a 2-year rat study. Effects in these studies included decreased body weight, signs of neurotoxicity and hepatotoxicity at the LOAELs. Standard uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability were applied. Residual uncertainty regarding potential susceptibility of the young and potential immunotoxicity was addressed with a 3-fold database uncertainty factor. Consequently, the *Pest Control Products Act* factor was reduced to 1-fold as discussed in the *Pest Control Products Act* Hazard Characterization section. Therefore, the composite assessment factor is 300.

$$\textbf{ADI} = \frac{\textbf{5.0 mg/kg bw/day}}{\textbf{300}} = \textbf{0.02 mg/kg bw/day}$$

The ADI provides a margin of 1250 to the LOAEL (25 mg/kg bw/day) for testicular effects noted in the specialized repeat-dose reproductive toxicity studies. The dose showing some response on immune parameters in a supplemental oral mouse study (0.4 mg/kg bw/day) approached the ADI thus supporting the need for a database uncertainty factor in the absence of a more definitive study.

3.2.4 Chronic Non-Cancer Dietary Exposure and Risk Assessment

The chronic dietary risk (from food and drinking water) was calculated by using the average consumption of different foods and drinking water, and the average residue values on those foods and drinking water. This estimated exposure to permethrin was then compared to the ADI. The ADI is an estimate of the level of daily exposure to a pesticide residue that, over a lifetime, is believed to have no significant harmful effects. When the estimated exposure is less than the ADI, the chronic dietary exposure is not of concern.

The chronic refined dietary risk assessment was conducted for the general population and all subpopulations using average residues from the same CFIA and PDP monitoring data used in the acute assessment and average anticipated residues from field trials or MRLs/tolerances for commodities for which no monitoring data were available. Residue adjustment factors were estimated from available field trials and metabolism data and used to account for residues of DCVA, MPBA and 3–PBA in commodities where these metabolites were identified as major residues. Policies from the PMRA and USEPA were used for crop translations when necessary. In addition, the following inputs were incorporated where available: percent crop treated (PCT) information in Canada and the United States; 100% crop treated for commodities for which no PCT information was available; available information on domestic production and import supply; and available experimental processing factors. DEEM-FCID default processing factors were used when experimental processing factors were not available. Drinking water contribution to the exposure was accounted for by direct incorporation of the highest 50-year average drinking water EEC point estimate obtained from water modelling (see Section 3.3), into the dietary exposure evaluation (DEEM-FCID).

The chronic exposure estimates for the general population and all subpopulations was 2% of the ADI or less. Chronic dietary exposure is, therefore, not of concern.

3.2.5 Cancer Potency Factor

Based on the weight of evidence, permethrin poses tumorigenic potential in humans. There was evidence of tumorigenicity in mice and rats in vivo in the form of an increased incidence of benign lung adenomas in female mice, hepatocellular adenomas in male mice and thyroid adenomas in female rats. A cancer potency factor (q_1^*) of 9.87×10^{-3} $(mg/kg\ bw/day)^{-1}$ was derived based on the combined incidence of lung adenomas and carcinomas in female mice treated with permethrin. This cancer potency factor was selected as it reflected the most conservative potency factor for the various tumour types.

3.2.6 Cancer Dietary Exposure and Risk Assessment

The dietary cancer risk (from food and drinking water) was conducted for the general population by using the same residues for chronic assessment as described in Section 3.2.4 and the 50-year average groundwater EEC point estimate obtained from water modelling (see Section 3.3).

The dietary cancer risk is determined by multiplying the estimated lifetime exposure by the cancer potency factor (q_1^*). A lifetime cancer risk that is equal or less than 1×10^{-6} (one-in-a-million) usually does not indicate a risk of concern for the general population when exposure occurs through pesticide residues in or on food and drinking water, or to otherwise unintentionally exposed persons. Based on the current use pattern, the lifetime cancer risk estimate from exposure to permethrin through food and drinking water for the general population is greater than 1×10^{-6}, indicating the need for risk mitigation. Drinking water was identified as the major risk driver. To lower drinking water exposure to permethrin resulting from Canadian agricultural uses, reducing the number of seasonal applications (i.e., reducing the maximum number of application from 6 to 5 for the use of permethrin on tomato) are proposed. With this proposed mitigation measure, the cancer risk from food and drinking water exposure is estimated as 1×10^{-6} for the general population and is not of concern. Drinking water accounts for approximately 25% of the total exposure.

3.3 Exposure from Drinking Water

3.3.1 Concentrations in Drinking Water

Estimated environmental concentrations (EECs) of permethrin in potential drinking water sources (groundwater and surface water) were generated using the Pesticides in Water Calculator (PWC) model which incorporates the Pesticide Root Zone Model version 5.0 (PRZM5) model (for surface water and groundwater) and the Variable Volume Water Model (VVWM) for surface water. PWC was run for a 50-year period. The groundwater concentrations calculated using PWC are average concentrations in the top 1 m of the water table. Surface water EECs are calculated using PRZM5 to simulate pesticide runoff from a treated field and VVWM to simulate the fate of the pesticide in the receiving water body. Pesticide concentrations in surface water were estimated in a vulnerable drinking water source, a small reservoir.

Permethrin transformation products, DCVA (*cis*- and *trans*- isomers), MPBA and 3-PBA, were included in the drinking water modelling. Four sets of model runs were done, to simulate the transformation of both cis- and trans-permethrin to both (*cis*- and *trans*-) DCVA, MPBA and 3-PBA. The daily EECs were added (after adjusting for the molecular weight of the transformation products) to obtain the combined EECs.

The highest daily water modelling EEC (6.23 µg/L from surface water) was used for the acute dietary risk assessment of permethrin and its transformation products in drinking water. To lower the drinking water exposure and reduce the potential dietary (cancer) risk to an acceptable level, 5 applications of 140 g a.i./ha were considered for tomato instead of the 6 applications indicated on the current label.

The highest 50-year average EEC from water modelling (1.83 µg/L from groundwater modelled based on 5 applications on tomato) was used as an estimate for the chronic and cancer dietary risk assessments of permethrin and its transformation products in drinking water. Since groundwater EECs were generated based on a reduced number of applications for tomato, this change needs to be reflected on the product labels, where applicable.

3.3.2 Drinking Water Exposure and Risk Assessment

Drinking water exposure estimates were combined with food exposure estimates. The daily surface water EEC point estimate was incorporated directly in the acute dietary assessment and the 50-year average groundwater EEC point estimate was incorporated directly in the chronic and cancer dietary assessments. Please refer to Sections 3.2.2, 3.2.4 and 3.2.6.

3.4 Occupational and Residential Risk Assessment

Occupational and residential risk is estimated by comparing potential exposures with the most relevant endpoint from toxicology studies to calculate a margin of exposure (MOE). This is compared to a target MOE incorporating uncertainty factors protective of the most sensitive subpopulation. If the calculated MOE is less than the target MOE, it does not necessarily mean that exposure will result in adverse effects, but mitigation measures to reduce risk would be required.

3.4.1 Toxicological Endpoints for Residential and Occupational Exposure

3.4.1.1 Dermal Exposure

For **short-, intermediate- and long-term dermal risk assessment in all populations**, a systemic NOAEL of 500 mg/kg bw/day was selected from the 21-day dermal toxicity study in rats which was the highest dose tested. At this dose level, an initial decrease in body weight and adaptive effects on the liver occurred while no evidence of neurotoxicity was noted. A target MOE of 300 was derived for the critical endpoint. This includes uncertainty factors of 10-fold for interspecies extrapolation, 10-fold for intraspecies variability and a 3-fold database uncertainty factor for concerns related to potential sensitivity of the young and evidence of immunotoxicity by the dermal route. For residential scenarios, the *Pest Control Products Act* factor was reduced to 1-fold as discussed in the *Pest Control Products Act* Hazard Characterization Section.

3.4.1.2 Inhalation Exposure

The most appropriate study for **short-, intermediate- and long-term inhalation risk assessment in all populations** is the 13-week inhalation toxicity study in rats in which a NOAEC of 0.25 mg/L (65 mg/kg bw/day) for permethrin was derived based on signs of neurotoxicity at 0.50 mg/L (130 mg/kg bw/day). A target MOE of 300 was selected, which includes uncertainty factors of 10-fold for interspecies extrapolation, 10-fold for intraspecies variability and a 3-fold database uncertainty factor for concerns related to potential sensitivity of the young and potential immunotoxicity. For residential scenarios, the *Pest Control Products Act* factor was reduced to 1-fold as discussed in the *Pest Control Products Act* Hazard Characterization Section.

3.4.1.3 Non-Dietary Incidental Oral Ingestion

For assessment of **short-term non-dietary (incidental) oral exposure**, a $BMDL_{20}$ of 22.95 mg/kg bw from an acute oral neurotoxicity study conducted with permethrin was selected, based on reduced motor activity in adult rats (PMRA No. 2078450). This $BMDL_{20}$ was considered most relevant since it is based on a sensitive endpoint and was derived from a study of relevant route and duration of exposure. A target MOE of 300 was selected which includes uncertainty factors of 10-fold for interspecies extrapolation, 10-fold for intraspecies variability and a 3-fold database uncertainty factor for concerns related to potential sensitivity of the young and potential immunotoxicity. The *Pest Control Products Act* factor was reduced to 1-fold as discussed in the *Pest Control Products Act* Hazard Characterization Section.

For assessment of **intermediate- and long-term non-dietary (incidental) oral exposure**, a NOAEL of 5.0 mg/kg bw/day was selected from the following co-critical toxicity studies: the 4-week mouse study with offspring assessment, a 90-day dog study, a 52-week dog study and a 2-year rat study, based on decreased body weight, signs of neurotoxicity and hepatotoxicity. A target MOE of 300 was selected which includes uncertainty factors of 10-fold for interspecies extrapolation, 10-fold for intraspecies variability and a 3-fold database uncertainty factor for concerns related to potential sensitivity of the young and potential immunotoxicity. The *Pest Control Products Act* factor was reduced to 1-fold as discussed in the *Pest Control Products Act* Hazard Characterization Section.

3.4.1.4 Cancer Risk Assessment

Based on the weight of evidence, permethrin poses tumorigenic potential in humans. There was evidence of tumorigenicity in mice and rats in vivo in the form of an increased incidence of benign lung adenomas in female mice, hepatocellular adenomas in male mice and thyroid adenomas in female rats. A cancer potency factor of 9.87×10^{-3} $(mg/kg\ bw/day)^{-1}$ was derived based on the combined incidence of lung adenomas and carcinomas in female mice orally treated with permethrin. This cancer potency factor was selected as it reflected the most conservative potency factor for the various tumour types. The cancer potency factor was considered relevant to all routes of exposure.

3.4.1.5 Dermal Absorption

For the non-cancer risk assessment, a dermal absorption value is not required since the toxicological point of departure was derived from a dermal study. A dermal absorption value was required for the cancer assessment since the potency factor was derived from an oral study. A dermal absorption of 12% (monkey forearm, Sidon, 1988) was considered appropriate to estimate dermal absorption for permethrin for typical pesticide application and postapplication scenarios.

3.4.2 Non-Occupational Exposure and Risk Assessment

Non-occupational (residential) risk assessment involves estimating risks to the general population, including adults, youth and children, during or after pesticide application.

The USEPA has generated standard default assumptions for developing residential exposure assessments for both applicator and postapplication exposures when chemical- and/or site-specific field data are limited. The assumptions and algorithms may be used in the absence of, or as a supplement to, chemical- and/or site-specific data, and generally result in high-end estimates of exposure. These assumptions and algorithms relevant to the permethrin re-evaluation are outlined in the USEPA Standard Operating Procedures (SOP) for Residential Pesticide Exposure Assessments (2012) in the following sections:

- Section 3: Lawns and Turf
- Section 4: Gardens and Trees
- Section 5: Outdoor Fogging/Misting Systems
- Section 7: Indoor Environments
- Section 8: Treated Pets

3.4.2.1 Residential Applicator Exposure and Risk Assessment

A residential applicator is an individual (≥16 years old) who applies a domestic-class permethrin product in and around the home or directly to animals. Residential applicators are assumed to be wearing shorts, short-sleeve shirts, shoes, and socks during application. The residential applicator has the potential for short-term exposure (1-30 days) when applying products containing permethrin.

Based on current labels, the major scenarios identified were:

- Applying liquid formulations using manually pressurized handwand, and trigger sprayer to lawns and turf and gardens and trees.
- Applying ready-to-use formulations using aerosol sprays to lawns and turf and gardens and trees.
- Applying pressurized sprays and foggers to outdoor areas.
- Applying liquid formulations using manually pressurized handwand, trigger sprayer, and paint brush to indoor areas.
- Applying ready-to-use formulations using aerosol sprays as surface sprays, space sprays, and foggers to indoor areas.
- Applying solid formulations as foggers to indoor areas.
- Applying ready-to-use formulations as foam or topical sprays to dogs and cats or spot-on treatment for dogs.

- Applying ready-to-use formulations using a trigger spray, cloth, or aerosol spray to horses.

Data were not available to assess exposure when using hand-held electric mist sprayers/blowers.

The calculated MOEs and cancer risks for residential applicators showed no risks of concern for uses that could be assessed. Cancer risks for trigger spray bottle application to horses were slightly higher than the threshold. However, for this use the maximum application rate along with a conservative (i.e. upperbound) estimate for number of horses treated per day were used to calculate risk. Since the cancer risks were approaching the acceptable level, the cancer risk was deemed acceptable based on the conservatisms in the risk assessment. Therefore, there were no risks of concern identified for residential applicators. As application exposure from hand-held mist sprayers/blowers could not be assessed label directions are proposed prohibiting application using these types of equipment. The results of the risk assessment are summarized in Appendix II, Tables 7-8.

3.4.2.2 Residential Postapplication Exposure and Risk Assessment

Residential postapplication exposure occurs when an individual is exposed through dermal, inhalation, and/or incidental oral (non-dietary ingestion) routes as a result of being in a residential environment or by contacting a treated animal that has been previously treated with a pesticide. For permethrin, the area or animal could have been treated by a residential applicator using a domestic-class product or a commercial applicator hired to treat the residential area or animal.

While exposure may occur for people of all ages, adults (>16 years old), youth (11 <16 years old), and children (6 <11 years old, and 1 <2 years old) have been chosen as the index lifestages to assess based on behavioural characteristics and the quality of the available data. For many scenarios it is assumed that younger children (i.e. 1 <2 years old) would have higher exposure in these areas when playing or engaging in the types of activities associated with this lifestage (e.g. crawling or mouthing) than would older children (i.e. > 6 years old). For these scenarios, children 2 to <11 years were not assessed separately because their exposure is expected to be lower.

There is potential for intermittent short-term exposure to adults, youth (11 to <16 years old), and children (6 to <11 years old and 1 to <2 years old) through contact with transferable residues following applications of permethrin to indoor and outdoor environments and to pets. Adults, youth and children have the potential for postapplication dermal exposure; children (1 to <2 years old) also have the potential for incidental oral exposure.

Due to seasonality of most pests (e.g. fleas) listed on the label; postapplication exposure is expected to be intermittent short-term (1-30 days). The following scenarios were assessed for short-term postapplication exposure for residential use of products containing permethrin:

- Adults, youth, and children (1 <2 years old) dermal exposure resulting from activities on lawns and turf.

- Children (1 <2 years old) incidental oral exposure from treated lawns and turf.
- Adults youth, and children (6 <11 years old) dermal exposure resulting from activities in gardens and trees.
- Adults, youth, and children (1 <2 years old) dermal and inhalation exposure resulting from outdoor aerosol space sprays.
- Children (1 <2 years old) incidental oral exposure from outdoor aerosol space sprays.
- Adults, youth, and children (1 <2 years old) dermal and inhalation exposure resulting from activities indoors after indoor surface and space sprays.
- Children (1 <2 years old) incidental oral exposure resulting from indoor surface and space sprays.
- Adult, youth, and children (1 <2 years old) dermal exposure resulting from exposure to treated pets.
- Children (1 <2 years old) incidental oral exposure from treated pets.

For bedbugs, there may be the potential for long-term exposure (>180 days). The following scenarios were assessed for long-term postapplication exposure for residential use of products containing permethrin for bedbugs.

- Adult, youth, and children (1 to <2 years old) dermal and inhalation exposure in indoor environments.
- Incidental oral (hand-to-mouth) exposure to children (1 to <2 years old) in indoor environments.

Since label directions prohibiting application by hand-held misting systems in animal barns are proposed (see Section 3.4.3), postapplication exposure from mists was not assessed. However, postapplication exposure due to application in animal barns using other types of application equipment was assessed under the indoor environment scenario.

It was assumed that individuals would contact previously treated surfaces and pets on the same day the pesticide is applied.

Postapplication dermal exposure can result from pesticide residue transfer to the skin of individuals who contact previously treated surfaces on lawns, gardens, trees, pets, and indoors, and during activities such as recreation, gardening, or housework.

For inhalation exposure in indoor environments, estimates of exposure are specified in the 2012 USEPA Residential SOPs for both aerosol and vapours. Aerosols are a spray of fine particles, typically present after space spray applications, which tend to settle out of the air after a certain period of time. Vapours occur when the pesticide volatilizes from a surface after application and can occur from all types of pesticide application. Inhalation exposure can occur from either

indoor or outdoor aerosol space sprays, by breathing air containing pesticide vapours or aerosols. Postapplication inhalation exposure while performing activities in previously treated lawns and gardens is expected to be low for permethrin due to the combination of a low vapour pressure and the expected dilution in outdoor air. Potential long-term exposure via the inhalation route exists for residents living in homes treated for termites with permethrin. However due to the low vapour pressure of permethrin, it is unlikely to volatilize in typical indoor conditions. Therefore, a quantitative inhalation postapplication risk assessment was not conducted.

Incidental oral exposure occurs when pesticide residues are transferred to the hands of children playing on treated lawns, indoor surfaces or with treated pets, and are subsequently ingested as a result of hand-to-mouth (HtM) transfer. Residues can also be transferred to objects in treated areas (e.g. a child's toy) and subsequently ingested as a result of object-to-mouth transfer. Soil can also be ingested while playing on treated lawns as a result of normal mouthing activities.

For the non-cancer risk assessment, target MOEs were achieved for all scenarios, except for the following:

- Lawns and turf application: Dermal and incidental oral exposure at the highest application rate (target MOEs were obtained at the lower application rate).

- Indoor solid fogger application: Inhalation exposure.

Therefore, to mitigate risk, label directions are proposed that restrict the application rate for lawns and turf to the lower application rate and indoor solid foggers are proposed for cancellation.

For the postapplication cancer risk assessment, adequate data are not available to conduct a refined (or more precise) estimate of exposure. Although the algorithms in the USEPA Residential SOPs were used, critical information required for a cancer assessment (e.g. potential number of days of exposure and years of exposure) are not available. Also, the Residential SOPs provide very conservative (i.e. high-end) estimates of exposure intended to be used for non-cancer risk assessments. When using the Residential SOPs and assuming adults have 63 years of exposure over a 78 year lifetime for up to a total of 30 days per year, the potential cancer risk was greater than 1×10^{-6} for the following scenarios:

- Lawns and turf applications: Dermal and incidental oral exposure at the highest application rate (risks were mitigated using the lower application rate).

- Gardens and trees: Dermal exposure.

- Outdoor aerosol space spray: Dermal exposure.

- Indoor environments: Dermal exposure due to broadcast, perimeter, crack and crevice and solid fogger applications. Inhalation exposure for aerosol space spray and solid fogger applications.

- Mosquito abatement: Inhalation exposure.

When determining potential risk mitigation for cancer risks, the degree of conservatism in the Residential SOPs algorithms and the assumptions used in exposure and risk assessment were taken into account, as were the results from the aggregate risk assessment (Section 3.5). Based on these considerations, the following risk mitigation measures are proposed:

- Label directions are proposed to restrict the application rate for lawns and turf to the lower application rate.
- Indoor solid foggers are proposed for cancellation.
- Indoor broadcast applications are proposed for cancellation.

The results of the risk assessment are summarized in Appendix II, Tables 9-14.

3.4.3 Occupational Exposure and Risk Assessment

There is potential for exposure to permethrin in occupational scenarios from workers handling permethrin products during application processes, from workers entering treated areas, contacting treated animals, or wearing treated military uniforms.

3.4.3.1 Occupational Applicator Exposure and Risk Assessment

For commercial-class products, there are potential exposures for mixers, loaders, and applicators (MLAs). Based on typical use patterns, the major scenarios identified were:

- Mixing and loading of liquids
- Applying liquids by air
- Applying liquids by airblast
- Applying liquids by groundboom
- Applying liquids by right-of-way sprayers
- Applying liquids by mist blowers
- Applying liquids by electric mist sprayers
- Mixing, loading, and applying liquids by mechanically pressurized handgun sprayer
- Mixing, loading, and applying liquids by manually pressurized handwand sprayer
- Mixing, loading, and applying liquids by backpack sprayer
- Applying pressurized products by aerosol
- Applying pressurized products by fogger

- Applying liquids and aerosols by cloth or pour-on treatment
- Applying liquids by back rubber
- Applying slow release generators by ear tag
- Applying liquids by spot-on treatment
- Applying liquids using a spray box for wood treatment
- Applying liquids by rod or sub-slab injector

The exposure estimates for mixer/loaders and applicators are based on different levels of personal protective equipment (PPE) and engineering controls:

A. Baseline PPE - long pants, long sleeved shirts and chemical-resistant gloves (unless specified otherwise). For groundboom application, this scenario does not include gloves, as the data quality was better for non-gloved scenarios than gloved scenarios.

B. Mid-Level PPE – cotton coveralls over long pants, long sleeved shirts and chemical-resistant gloves.

C. Chemical-resistant Headgear – chemical-resistant headgear that covers the neck (e.g. Sou'Wester hat, rain hat).

No appropriate chemical-specific handler exposure data were available for permethrin. Therefore, dermal and inhalation exposure for occupational applicators were estimated using data from the Pesticide Handlers Exposure Database (PHED), the Agricultural Handler Exposure Task Force (AHETF), the Outdoor Residential Exposure Task Force (ORETF), and the Sapstain Industry Group (SIG).

The PHED version 1.1 is a compilation of generic mixer/loader and applicator passive dosimetry data with associated software which facilitates the generation of scenario-specific exposure estimates based on formulation type, application equipment, mix/load systems and level of personal protective equipment. The open cab airblast scenario from AHETF and the hose-end sprayer scenario from ORETF were used in the risk assessment. Inhalation exposures were based on light inhalation rates (17 L/min) except for backpack applicator scenarios, which are based on moderate inhalation rates (27 L/min).

The Sapstain Industry Group (SIG) was formed with the objective of providing exposure data for applications of antisapstains. The SIG conducted passive dosimetry worker exposure studies to measure the potential exposure of sawmill workers that are exposed to antisapstain chemicals. The Phase IV study was considered to be acceptable as a surrogate for use in the determination of potential exposure to pesticides for pilers, clean-up crew, and maintenance workers involved in the antisapstain treatment of lumber.

No data were available to assess exposure when using foggers and hand-held mist blowers. For spot-on treatment to animals (dogs, cats, horses), a separate assessment for workers was not conducted. Risks for the commercial applicator were assumed to be similar to or less than residential applicator risk, due to the longer exposure duration for the residential scenario.

Workers applying permethrin have the potential for short-, intermediate- and/or long-term durations of exposure. For the cancer risk assessment agriculture workers were assumed to have a working career of 40 years, resulting in 40 years of exposure over a 78 year lifetime. Applicators were assumed to be exposed for up to a total of 30 days per year. Military personnel were assumed to have a working career of 16 years, resulting in 16 years of exposure over a 78 year lifetime, and applicators were assumed to be exposed for up to 10 days per year based on information provided from the Department of National Defence (DND). Non-agricultural pest control workers were assumed to have a working career of 16 years, resulting in 16 years of exposure over a 78 year lifetime, and applicators were assumed to be exposed for up to 30 days per year based on study and survey information.

The calculated MOEs and cancer risks for agricultural and military uniform applicators showed no risks of concern for uses provided proposed mitigation measures are implemented. The calculated MOEs and cancer risks for commercial applicators in residential areas showed no risks of concern for most uses provided proposed mitigation measures are implemented. Cancer risks for airblast application for mosquito abatement and mechanically pressurized handgun application to lawns and turf and gardens and trees were slightly higher than the threshold even when considering the proposed mitigation measures. However, for these uses the maximum application rate along with a conservative estimate for area treated per day were used to calculate risk. Since the cancer risks were approaching the acceptable level, the cancer risk was deemed acceptable based on the conservatisms in the risk assessment. Therefore, there were no risks of concern for commercial applicators, provided proposed mitigation measures are implemented. As application exposure from foggers and hand-held mist blowers could not be assessed; label directions prohibiting use of these types of application equipment are proposed. The results of the risk assessment are summarized in Appendix II, Tables 1-4.

3.4.3.2 Occupational Postapplication Exposure and Risk Assessment

There are four broad categories of potential occupational postapplication exposure scenarios: agricultural, structural, livestock and pets, and military uniforms.

Agricultural Sites

Agricultural scenarios refer to workers entering treated fields, nurseries, forest and woodlots, greenhouses, and mushroom houses to conduct agronomic activities involving foliar contact (for example, pruning, thinning, harvesting, or scouting). Based on the permethrin use pattern there is potential for short- to intermediate-term exposure (>1 day to several weeks) for workers entering areas of field crops treated with permethrin and long-term exposure (several months) for workers entering greenhouses and mushroom houses.

Potential dermal exposure to postapplication workers was estimated using updated activity-specific transfer coefficients (TCs) and dislodgeable foliar residue (DFR) or turf transferable residue (TTR) data. The DFR and TTR refer to the amount of residue that can be dislodged or transferred from a surface, such as leaves of a plant or turf. The TC is a measure of the relationship between exposure and DFRs/TTRs for individuals engaged in a specific activity, and is calculated from data generated in field exposure studies. The TCs are specific to a given crop and activity combination (for example, hand harvesting apples, scouting late season corn) and reflect standard agricultural work clothing worn by adult workers. Activity-specific TCs from the Agricultural Re-Entry Task Force (ARTF) were used. Postapplication exposure activities for agricultural crops include (but are not limited to): harvesting, pruning, scouting and thinning. For more information about estimating worker postapplication exposure refers to PMRA's regulatory proposal PRO2014-02 (*Updated Agricultural Transfer Coefficients for Assessing Occupational Exposure to Pesticides*).

A chemical-specific DFR study was submitted to the PMRA for the re-evaluation of permethrin. This study was conducted on peaches and was used for orchards/trees. The submitted study on orchard crops showed a lower peak DFR value than the default value, and thus, the default peak DFR value was used for all outdoor crops other than orchard crops, but with the dissipation value derived from this study. The following values were used in the risk assessment:

- A peak value of 18% of the application rate with a dissipation rate of 6% per day was used for DFR for orchards and trees.
- A default peak value of 25% of the application rate with a dissipation rate of 6% per day was used for DFR for outdoor crops other than orchards and trees
- A default peak value of 25% was used with a default dissipation rate of 2.3% was used for DFR for greenhouse ornamental crops.
- A default peak value 25% was used with a default dissipation rate of 0% was used for DFR for greenhouse vegetable crops.
- A default peak value of 1% of the application rate with a dissipation rate of 6% per day was used for TTR.

Exposure would be predominantly dermal for workers performing postapplication activities in crops treated with a foliar spray. Based on the vapour pressure of permethrin, inhalation exposure is not likely to be of concern provided that the minimum 12 hour restricted entry interval is followed.

For agricultural workers entering a treated site, restricted entry intervals (REIs) are calculated to determine the minimum length of time required before workers can enter after application to perform tasks involving hand labour. An REI is the duration of time that must elapse before residues decline to where there are no risks of concern for postapplication worker activities (in the case of permethrin, performance of a specific activity that results in exposures above the target MOE of 300 and below the acceptable cancer risk threshold of 1×10^{-5} is not of concern).

The calculated MOEs and cancer risks for postapplication exposure in agricultural sites are not of concern for most uses provided a 12 hour REI is followed. REIs greater than 12 hours are required for some crops and activities and range from 2-15 days. These REIs are considered to be agronomically feasible. The results of the risk assessment are summarized in Appendix II, Tables 5- 6.

There is potential for postapplication exposure in mushroom houses. Currently, there are no data to estimate exposure to workers entering treated mushroom houses. No data are available to determine transferable residues of permethrin from treated surfaces, or air concentrations for mists/aerosols immediately after application. In addition, the extent of postapplication activities is unknown. As a postapplication exposure assessment could not be conducted for mushroom houses, the use is proposed for cancellation.

Structural Application Sites

There is potential exposure to workers entering treated livestock housing including poultry houses, commercial or residential sites.

Possible occupational postapplication worker scenarios include:

- Commercial applicator or pest control operator returning to treated sites;
- Workers entering treated feedlots, dairies, barns, and livestock housing;
- Workers in other treated commercial, industrial or institutional locations;
- Workers in treated hotels and motels;
- Workers in treated boats, buses, ships, planes, or trains;
- Workers in treated nursing homes and hospitals;
- Workers in treated restaurants.

Similar to agricultural scenarios, postapplication inhalation exposure is not expected to be of concern due to the low vapour pressure of permethrin, and assuming entry does not occur until residues have deposited or dried.

Postapplication exposure in feedlots is expected to be low due to the lack of postapplication activities where workers may come in contact with treated surfaces.

For most of these scenarios, a separate quantitative assessment for postapplication workers was not conducted. It was assumed that risks to postapplication workers in these scenarios would be similar to or less than residential postapplication risks, since time spent in residential areas is assumed to be longer than time spent working. This assumption is unlikely to underestimate occupational postapplication exposure. The residential assessment is discussed in Section 3.4.2. Risk mitigation measures for residential areas would also be required for these scenarios.

Animal Applications (Livestock and Pets)

Similar to other scenarios, dermal exposure is the primary route of concern following applications to livestock and pets, provided that exposure would occur after residues have dried.

A quantitative postapplication risk assessment was not conducted for livestock uses as the level of postapplication interaction with the animals is expected to be minimal.

For veterinarians or workers handling treated pets, a separate quantitative assessment was not conducted. It was assumed that risks to postapplication workers would be similar to or less than the risks for residential postapplication risks, due to the longer exposure duration for the residential scenario. The residential assessment is discussed in Section 3.4.2. No risk mitigation measures beyond what is currently on the label were required for this use.

Military Uniforms

Dermal exposure is the primary route of concern following applications to military uniforms from pesticide residue transfer to the skin of individuals who wear treated uniforms. There is low inhalation exposure potential based on the low vapour pressure of permethrin. Chemical-specific residue transfer and laundering studies were submitted to the PMRA for the re-evaluation of permethrin. These studies were conducted on military clothing treated with permethrin. A transfer rate of 1.15% per day and laundering loss ranging from 1.55% to 30% depending on the timing of the laundering were used in the risk assessment.

A quantitative assessment for postapplication exposure to military personnel was conducted. The dermal exposure and non-cancer and cancer risk assessments for military clothing show no risks of concern. An MOE of 540 for military workers wearing uniforms treated using the aerosol formulation, and an MOE of 1800 for military workers wearing uniforms treated with the liquid formulation was calculated. For military workers wearing uniforms treated with permethrin using the aerosol formulation, or the liquid formulation, cancer risks were 5×10^{-6} and 7×10^{-6}, respectively.

These MOEs and cancer risks for postapplication exposure when wearing military uniform showed were not of concern provided that exposure would occur after residues have dried.

3.5 Aggregate Risk Assessment

Aggregate exposure is the total exposure to a single pesticide that may occur from food, drinking water, residential, and other non-occupational sources, and from all known or plausible exposure routes (oral, dermal and inhalation).

3.5.1 Toxicology Endpoint Selection for Aggregate Risk Assessment

For **acute aggregate risk assessment** of the general population (including pregnant women, infants and children), the selected toxicological endpoint was motor activity. For oral exposure, the $BMDL_{20}$ (benchmark dose 95% lower confidence limit at the 20% effect level) of 22.95 mg/kg bw from an acute oral neurotoxicity study conducted with permethrin was selected. A target MOE of 300 was selected with a 10-fold uncertainty factor for interspecies extrapolation, a 10-fold uncertainty factor for intraspecies variability and a 3-fold database uncertainty factor for

concerns related to potential sensitivity of the young and potential immunotoxicity. The *Pest Control Products Act* factor was reduced to 1-fold as discussed in the *Pest Control Products Act* Hazard Characterization section. With regards to the dermal and inhalation routes, there were no effects on motor activity following repeated dosing. As a result, it was considered appropriate to not include the dermal and inhalation routes in the acute-term aggregate risk assessment.

For **short- and intermediate-term aggregate risk assessment** of the general population (including pregnant women, infants and children), the selected toxicological endpoints were clinical signs of neurotoxicity (i.e. tremors). For oral exposure, the NOAEL of 5 mg/kg bw/day from the 90-day toxicity study in rats was selected. For inhalation exposure, the NOAEL of 65 mg/kg bw/day from the 13-week inhalation toxicity study in rats was selected. For both the oral and inhalation routes of exposure, a target MOE of 300 was selected. This target MOE includes a 10-fold uncertainty factor for interspecies extrapolation, a 10-fold uncertainty factor for intraspecies variability and a 3-fold database uncertainty factor for concerns related to potential sensitivity of the young and potential immunotoxicity. The *Pest Control Products Act* factor was reduced to 1-fold as discussed in the *Pest Control Products Act* Hazard Characterization section. With regards to the dermal route, there were no signs of neurotoxicity noted following repeated dermal dosing, up to a limit dose of 500 mg/kg bw/day. As a result, it was considered appropriate to not include the dermal route in the short- and intermediate-term aggregate risk assessment.

For **long-term aggregate risk assessment** of the general population (including pregnant women, infants and children), the selected toxicological endpoint of concern was liver toxicity. For oral exposure, a NOAEL of 5 mg/kg bw/day was selected from the 52 week toxicity study in dogs. For dermal exposure, a NOAEL of 500 mg/kg bw/day from the 21-day dermal toxicity study in rats was selected. For inhalation exposure, the NOAEL of 65 mg/kg bw/day from the 13-week inhalation toxicity study in rats was selected. For all of these routes of exposure, a target MOE of 300 was selected which includes a 10-fold uncertainty factor for interspecies extrapolation, 10-fold uncertainty factor for intraspecies variability and a 3-fold database uncertainty factor for concerns related to potential sensitivity of the young and potential immunotoxicity. The *Pest Control Products Act* factor was reduced to 1-fold as discussed in the *Pest Control Products Act* Hazard Characterization section.

For the aggregate risk assessment for cancer, the cancer potency factor of 9.87×10^{-3} (mg/kg bw/day)$^{-1}$, based on the combined incidence of lung adenomas and carcinomas in female mice orally treated with permethrin, was considered relevant for all routes of exposure.

3.5.2 Aggregate Risk Assessment Using Standard Approaches

In an aggregate risk assessment, the combined potential risk associated with food, drinking water and various residential exposure pathways is assessed. A major consideration is the likelihood of co-occurrence of exposures and durations of exposures. Additionally, only exposures from routes that share common toxicological points of departure can be aggregated.

With regards to acute aggregate risk for permethrin, as noted in Section 3.5.1, only the oral route of exposure is relevant. Therefore, aggregation with potential acute dermal and inhalation exposures is not required. Aggregation may be possible for acute dietary exposure with incidental oral exposure in children from residential uses. However, co-occurrence of two high-end exposure pathways on the same day is unlikely. Therefore, an acute aggregate risk assessment was not required.

For short- and intermediate-term aggregate risk, oral and inhalation routes are most relevant (Section 3.5.1). However, for most residential scenarios dermal exposure was the predominant route for adults, with both oral and dermal routes predominant for children. There were limited scenarios with co-occurrence of oral or inhalation exposures (e.g. outdoor aerosol space sprays, mosquito abatement, and indoor environments). Aggregation with dietary exposure and residential incidental oral or inhalation exposures was conducted as appropriate.

For long-term aggregate risk, all three routes of exposure are relevant and pathways of exposure with these routes were aggregated when there was likelihood of co-occurrence. For example, long term dermal, inhalation, and incidental oral exposure in children from bedbug applications were aggregated with chronic dietary exposures.

For the aggregate cancer assessment, all three routes of exposure are relevant. However, for most residential scenarios adequate data were not available using standard approaches (see Section 3.4.2). Therefore, aggregate cancer risk is considered further using biological monitoring data (see Section 3.5.3).

Individual scenarios which did not have risks of concern were aggregated to determine whether aggregation of exposures would result in risks of concern. Aggregate assessments were conducted for various populations as follows: children (1 < 2 years old) since they could have both incidental oral and inhalation exposure following application in residential areas and to animals, as well as dietary exposure; adults since they could have both applicator and postapplication dermal and inhalation exposure; following bedbug applications, long term aggregate exposure to children (1< 2 years old) from incidental oral, dermal, inhalation, and dietary exposures and adults from dermal, inhalation, and dietary exposures. A summary of co-occurring exposures is presented in Appendix II Table 15.

No risks of concern were identified for the non-cancer aggregate risk assessment. The results of the risk assessment are summarized in Appendix II, Table 16. The aggregate cancer risk assessment was based on biological monitoring data (see Section 3.5.3).

For the permethrin treated military uniform scenario, the aggregate non-cancer risk assessment resulted in MOEs of ≥490 for military personnel both treating and wearing permethrin-treated uniforms. The aggregate cancer risk assessment shows a cancer risk of $\leq 7 \times 10^{-6}$. Therefore, there were no risks of concern for this use, given that the cancer risk is well below the threshold of concern (i.e., 1×10^{-5}).

3.5.3 Aggregate Risk Assessment Using Human Biological Monitoring Data

Biological monitoring or biomonitoring is a method of assessing exposure to a pesticide by measuring the pesticide or its metabolites in biological media, such as urine or blood. Compared to ambient monitoring, biological monitoring has the advantage that it provides an integrated estimate of exposure through all relevant routes (inhalation, dermal and oral) and by all possible pathways (for example, food, drinking water and indoor uses) and reflects behavioural and physical sources of variability. It differs from the standard approach for aggregate human health risk assessments, in which exposure models and algorithms are used to estimate route-specific exposures using measurements of pesticide concentrations in the environment or what is deposited on the skin, inhaled, and/or consumed for specific scenarios.

Human biomonitoring (HBM) data are considered to be refined since they are reflective of the 'real-life' use of chemicals and, in the case of population biomonitoring surveys, would represent aggregate risk for the general population. Therefore, HBM data may be used when evaluating aggregate exposure to a pesticide to support risk estimates generated using PMRA's standard approach for human health risk assessments.

HBM data from the Canadian Health Measures Survey (CHMS; cycles 1 & 2; 2007-2011) and the Maternal-Infant Research on Environmental Chemicals – Child Development (MIREC CD-plus; 2013-2014[4]) were considered in the permethrin re-evaluation.

The CHMS is an on-going, nationally representative health measures survey that has been conducted by Statistics Canada, in partnership with Health Canada and the Public Health Agency of Canada, since 2007. The cross-sectional survey collects information from Canadians such as physical measures (for example, height and weight) and general health (for example, blood pressure and fitness), as well as a biomonitoring component. It follows a similar study design to the US National Health and Nutritional Examination Survey (NHANES) biomonitoring component. In Cycle 1 of the CHMS (2007-2009), blood and spot urine samples were collected from approximately 5,600 Canadians, 6-79 years old. In Cycle 2 (2009-2011), children as young as 3 years old were included. Pyrethroid metabolites were included in the suite of compounds measured.

The MIREC study was a national-level multi-year study that recruited approximately 2,000 women in the first trimester of pregnancy from 10 cities across Canada [Arbuckle et al., 2013]. Women were followed over the course of their pregnancy to measure their exposure to environmental chemicals and examine potential health risks associated with these exposures. The Maternal-Infant Research on Environmental Chemicals-Child Development plus (MIREC-CD Plus) study, an off shoot of the MIREC study, recruited children between the ages of 15 months and 5 years of age from six of the most populous recruitment sites for the MIREC pregnancy cohort study. In addition to measuring their growth and neurodevelopment, blood and spot urine samples were collected from participating children. Approximately 200 urine samples from children under 3 years of age were analyzed. Data from the MIREC study were analysed at the

[4] Unpublished data from the Population Studies Division, Healthy Environments and Consumer Safety Branch, Health Canada.

request of PMRA under the Chemical Management Plan. Although the MIREC-CD Plus study aimed to collect urine from children that were 15 months to 3 years of age, there were no samples in the pyrethroid data set for children younger than 23 months.

Pyrethroid pesticides are rapidly metabolized and eliminated from the body through hydrolysis, oxidation, and conjugation. Following oral ingestion, inhalation or dermal exposure, pyrethroids are metabolized into carboxylic and phenoxybenzoic acids and excreted with urine. Pyrethroids and their metabolites can be measured in blood and urine, and are reflective of recent exposure to the parent compound or the metabolite in the environment.

Reverse dosimetry was used to estimate aggregate exposure to permethrin using the CHMS and MIREC-CD plus data. Reverse dosimetry (exposure reconstruction) is an approach that can be used to convert metabolite measurements in humans to estimates of human pesticide exposure (Sobus et al., 2010). In this approach, human biomonitoring data are back-calculated into systemic exposure estimates (µg/kg bw/day) using human pharmacokinetic data. The resulting systemic exposure estimates are then compared to hazard endpoints to estimate risk. Four human oral pharmacokinetic studies and one monkey intramuscular pharmacokinetic study were available for permethrin (Sidon et al, 1988; Gotoh et al., 1998; Cridland and Weatherley, 1977; Ratelle et al., 2015). Since there is no metabolite unique to permethrin alone that is excreted in the urine, the common metabolite of two isomeric 3-(2,2-dichlorovinyl)-2,2-dimethyl cyclopropane carboxylic acids (cis and trans-DCCA, also referred to as DCVA in this document) was used in the assessment. It was assumed that all of the DCCA was metabolized from permethrin. This is a conservative input (that is, resulting in upperbound estimate of exposure), since DCCA is a common metabolite of other pyrethroids (for example, cypermethrin and cyfluthrin) and is also formed in the environment following pyrethroid application. A human oral study by Ratelle, et al. (2015) was considered to be the most appropriate study to convert the measured concentration of urinary DCCA metabolites into an estimate of permethrin exposure (urinary excretion fraction). A urinary excretion fraction value of 36% (molar percent of total dose) was selected for cis + trans-DCCA, which was based on a urinary excretion fraction value of 10.3% for cis and 25.9% for trans-DCCA. The study was conducted in volunteers, followed informed consent procedures, and was approved by an independent ethics committee. The 95th percentile values (cis + trans) from CHMS and MIREC data were used to conduct the aggregate non-cancer risk assessment. For the cancer risk assessment, the arithmetic mean values (cis + trans) from CHMS data was used. For CHMS data, the upper 95% confidence bound of the 95th percentile or the arithmetic mean was used when the coefficient of the variation of that metric was greater than 33%. These are also considered to be conservative values. Equations for estimating daily urinary creatinine excretion were used to calculate daily exposure estimates. The CHMS and MIREC-CD plus metabolite data were normalized by each individual's body weight and extrapolated to a full day value using daily creatinine excretion values (determined for each individual based on their height and weight) using the equations from Mage et al. (2004).

There is uncertainty regarding whether the CHMS and MIREC-CD Plus biomonitoring studies were able to capture exposure peaks, given the short urinary elimination half-life of permethrin. To address this, four biomonitoring studies that monitored children following residential pesticide applications of permethrin were included in the analysis (Lu et al, 2009; Tulve, et al., 2008; Naeher, 2010; Wu, 2013). For the arithmetic means, the metabolite concentrations reported in CHMS and MIREC-CD Plus are in the range of those reported in the literature

studies. However, this is not the case for the 95th percentile values. CHMS and MIREC-CD Plus metabolite concentrations are generally less than those reported in the literature and suggest that CHMS and MIREC-CD Plus sampling regimes were not able to consistently capture the high concentrations of urinary metabolites which may be excreted shortly after exposure. As such, the 95th percentile values from the literature studies, where available, were also used in the analysis for the non-cancer risk assessments, where peak exposures need to be captured. In cancer risk assessments, the arithmetic mean is often used in the calculation as the average exposure over a lifetime is estimated. Since the arithmetic mean values from the literature studies and the CHMS are similar, there is high confidence in the use of arithmetic means for the cancer assessment.

The results of the aggregate risk assessments are shown in Appendix II, Tables17 and 18. Calculated MOEs are above the target MOE and are not of concern. Calculated cancer risks are slightly above the threshold of 1×10^{-6}. When considering the acceptability of aggregate cancer risk, the uncertainty and conservatisms of using the biomonitoring data are considered, as well as how this approach compares to the non-aggregate risk assessment using standard approaches along with the resulting mitigation measures proposed.

Although biomonitoring data is reflective of real-life use of permethrin products, there are a number of conservative assumptions in the use of these data to estimate lifetime cancer risk:

- The assumption that all of the measured DCCA metabolites are from exposure to permethrin is conservative, as DCCA is a metabolite of three widely used pyrethroids (permethrin, cypermethrin, and cyfluthrin).

- The DCCA metabolite also occurs from environmental degradation of permethrin, so some of the metabolites measured in the urine could be from direct exposure to these metabolites, rather than to permethrin.

- When metabolites were less than the limit of quantification (LOQ), ½ of the LOQ value was assumed. This is conservative as it assumes that everyone in the population has these metabolites in their urine (i.e. has been exposed to permethrin), which is likely not the case.

The aggregate cancer risk assessment using biomonitoring data supports the risk assessment conducted for dietary exposure. For aggregate exposure, the main pathway of exposure is considered to be though the diet. Although non-dietary exposures contribute to the aggregate exposure, these exposures are primarily episodic and have lower impact when considering the average exposures over a lifetime, as would occur from dietary exposure using the predictive model and standard approach (see Section 3.2.6). Based on the current use pattern, potential dietary cancer risks were above the threshold of 1×10^{-6} which is supported by the aggregate cancer assessment using biological monitoring data. However, with mitigation, dietary cancer risks were within the threshold 1×10^{-6}, indicating that mitigation proposed for the dietary cancer assessment would also mitigate the aggregate risk. In addition, the dietary cancer assessment was highly refined since it was based on surveillance data of permethrin residues in the food supply and other refinements. Compared to the conservatisms used for the aggregate assessment using biomonitoring data, the dietary cancer assessment may be more reflective of potential exposures to the Canadian population.

Besides mitigation for dietary exposure, mitigation measures to reduce exposures in residential scenarios were proposed for the non-aggregate risk (see Section 3.4.2.2). These include, but are not limited to removing all broadcast and fogging applications of permethrin, lowered rates for lawn and turf applications, and cancellation of solid fogger applications. Although these episodic exposures would have a lower impact on the aggregate cancer exposure, they would still contribute to reducing aggregate exposure and the potential aggregate cancer risk.

Therefore, based on the above conservatisms when using the biomonitoring data, the fact that the aggregate cancer risk is expected to be driven by the dietary cancer risk, which is acceptable with mitigation, along with the other mitigation measures being proposed to reduce residential exposures and the small degree to which the cancer threshold was exceeded, the aggregate cancer risk calculated using biomonitoring data was considered to be not of concern.

3.6 Cumulative Risk Assessment

The *Pest Control Products Act* requires the Agency to consider the cumulative effects of pest control products that have a common mechanism of toxicity. Permethrin belongs to a group of insecticides commonly known as the pyrethroids. Pyrethroids and pyrethrins have a common mechanism of toxicity wherein they all possess the ability to interact with voltage-gated sodium channels ultimately leading to neurotoxicity. Upon completion of the re-evaluation of the individual chemicals in the pyrethroid group, it will be determined whether a cumulative effects assessment is necessary and if so, this will be performed with all relevant chemicals of the common mechanism group.

4.0 Impact on the Environment

4.1 Fate and Behaviour in the Environment

Permethrin enters the terrestrial environment when it is used as an insecticide on a variety of field crops for the control of a broad spectrum of insect pests.

Based on its physicochemical properties, permethrin is highly insoluble and does not have the potential to volatilize from moist soil or water surfaces (Henry's Law Constant = 2.3×10^{-6} atm•m^3/mole). Hydrolysis is not an important route of transformation. Phototransformation is not expected to be an important route of transformation of permethrin on soil (SFO DT_{50} = 51 – 85 days) or in water (SFO DT_{50} = 106 days), however, there is evidence that photolysis of permethrin may be faster in seawater (SFO DT_{50} = 14 days). Based on an atmospheric half-life of 0.70 days (AOPWIN), long range transport is not expected to be a concern. No major transformation products were identified in laboratory studies under abiotic conditions.

In the terrestrial environment, permethrin is expected to be non-persistent to moderately persistent in aerobic soil. Under laboratory conditions, aerobic soil DT_{50} values range from 8 to 113 days; the *trans*-isomer of permethrin is shown to biotransform more readily than the *cis*-isomer. The majority of permethrin is shown to mineralize to CO_2; bound permethrin residues are shown to accumulate steadily in soil (14 – 59% of applied) before being further mineralized to CO_2. Under field conditions, permethrin demonstrates a similar degree of persistence in soil conditions; DT_{50} values from terrestrial field dissipation studies conducted in the US and Canada

range from 1 to 106 days. Only one major transformation product, *trans*-DCVA was identified from laboratory aerobic soil biotransformation studies. Minor transformation products included: phenoxybenzyl alcohol, 3-phenoxybenzoic acid and phenoxybenzoic aldehyde. Under anaerobic soil conditions, permethrin is expected to be moderately persistent to persistent (DT_{50} = 61 – 226 days). Compared to aerobic soil conditions, the accumulation of bound residues in anaerobic soil and mineralization in soil is relatively slow (3 – 12% and <1 – 5%, respectively). *Trans*-DCVA and 3-phenoxybenzoic acid were identified as major tranformation products from laboratory anaerobic biotransformation studies; minor transformation products included *cis*-DCVA, phenoxybenzyl alcohol and phenoxybenzoic aldehyde.

Permethrin is practically immobile in soil due to its strong adsorption onto soil particles (K_{oc} range: 28200 – 491000) and its insolubility in water (5.5 to 200 µg/L at 20-30°C). When taking into consideration the criteria of Cohen *et al.* (1984) and the groundwater ubiquity score (GUS) it was determined that permethrin is unlikely to leach through soil into groundwater. Soil column leaching experiments confirm that permethrin residues remains in the upper few inches of soil. In addition, there is no evidence of residue mobility under field conditions; (i.e., permethrin residues are predominantly confined within the upper 7.5 – 15 cm of soil). Permethrin residues, therefore, are not expected to leach into groundwater. However, laboratory adsorption data indicate that the transformation product DCVA is highly mobile in soil and 3-phenoxybenzoic acid is moderately to highly mobile in soil.

Permethrin can enter non-target aquatic environments through spray drift and run-off from the application site. Permethrin is highly insoluble in water and hydrolysis is not an important route of transformation. In aquatic environments, permethrin is expected to be slightly persistent under aerobic aquatic conditions (DT_{50} ranging from 38 – 43 days) and moderately persistent to persistent under anaerobic aquatic conditions (DT_{50} range from 113 – 175 days). Mineralization to CO_2 is slow under aerobic aquatic conditions (3 – 9% after 30 days) and under anaerobic aquatic conditions (1.6% after 90 days). Partitioning of permethrin to sediment dominates fate processes in aquatic systems. Only one major transformation product, *trans*-DCVA, was identified from laboratory aerobic and anaerobic aquatic biotransformation studies. Minor transformation products included *cis*-DCVA, 3-phenoxybenzoic acid and 3-phenoxybenzyl alcohol. Aquatic field studies demonstrate that permethrin dissipates relatively quickly in water. In lentic systems, permethrin is shown to dissipate from subsurface water with DT_{50} values ranging from 1.4 to 3.1 days; in lotic systems, permethrin dissipates in flowing water with half-lives ranging from 2 to 20 hours. The *cis*-isomer is shown to dissipate more quickly than the *trans*-isomer. The main removal mechanism from the water column is adsorption to suspended solids and to bottom sediments. In sediment, permethrin is immobile and shown to remain in the upper 0 to 2 inches. DT_{50} values of 118 to 256 and 18 to 62 days are reported for *cis* and *trans*-permethrin in pond sediment, respectively. The transformation products are shown to dissipate at a much slower rates in the water column than parent permethrin; 28, 22 and 7.5 days for *cis* and *trans*-DCVA, and 3-PBA, respectively. Transformation products were not detected in sediment.

The log octanol/water partitioning coefficient for permethrin (log k_{ow} = 6.1) suggests the potential for bioaccumulation in aquatic organisms. Laboratory derived bioconcentration factors (BCFs) in fish range from as low as 30 in muscle tissue to 1100 in viscera of fish. Once exposure to permethrin is stopped, residues clear from most tissues relatively quickly ($t_{1/2}$ = <1 to 6 days), except in lipid where it clears more slowly. Laboratory BCF values determined for other aquatic

taxa (algae, aquatic plants, invertebrates) vary widely and fall within the range of those reported for fish. Evidence of bioaccumulation in sediment dwelling aquatic invertebrates has also been observed (biota sediment accumulation factors, BSAFs, range from 0.31 to 10.9).

Field studies show a similar range of BAF values in fish (114 – 2714); however, these values are based on the minimum concentration detected in water and therefore, represent a worse-case estimate. Although there are uncertainties and variability (spatial and temporal) associated with field studies, the field BAF values are considered to offer a reasonable characterization of the exposure history of fish to permethrin and were found to be consistent with BCF values obtained under controlled laboratory conditions.

Evidence of permethin biomagnification (among other pyrethroids) has also been observed in marine wildlife; permethrin was the dominant pyrethroid measured in wild fish (38 – 56% of total pyrethroids) and dolphins (56 – 73% of total pyrethroids). The detection of permethrin in breast milk and placental tissues from pregnant and lactating female dolphins confirms that maternal transfer of permethrin and other pyrethroids occurs by both gestational and lactation pathways in non-agricultural areas. Bioaccumulation of permethrin is not expected to be a concern as it does not meet TSMP Track 1 criteria (>5000).

Evidence of preferential uptake of *cis*-permethrin compared to *trans*-permethrin was also observed in in some laboratory bioaccumulation studies and biomonitoring studies.

Environmental fate data for permethrin and its transformation products are summarized in Appendix V, Tables 1a-1c.

4.2 Environmental Risk Characterization

The environmental risk assessment integrates the environmental exposure and ecotoxicology information to estimate the potential for adverse effects on non-target species. This integration is achieved by comparing exposure concentrations with concentrations at which adverse effects occur. Estimated environmental exposure concentrations (EECs) are concentrations of pesticide in various environmental media, such as food, water, soil and air. The EECs are estimated using standard models which take into consideration the application rate(s), chemical properties and environmental fate properties, including the dissipation of the pesticide between applications. Ecotoxicology information includes acute and chronic toxicity data for various organisms or groups of organisms from both terrestrial and aquatic habitats including invertebrates, vertebrates, and plants. Toxicity endpoints used in risk assessments may be adjusted to account for potential differences in species sensitivity as well as varying protection goals (i.e., protection at the community, population, or individual level).

Initially, a screening level risk assessment is performed to identify pesticides and/or specific uses that do not pose a risk to non-target organisms, and to identify those groups of organisms for which there may be a potential risk. The screening level risk assessment uses simple methods, conservative exposure scenarios (for example, direct application at a maximum cumulative application rate) and sensitive toxicity endpoints. A risk quotient (RQ) is calculated by dividing the exposure estimate by an appropriate toxicity value (RQ = exposure/toxicity), and the risk quotient is then compared to the level of concern (LOC). If the screening level risk quotient is

below the level of concern, the risk is considered negligible and no further risk characterization is necessary. If the screening level risk quotient is equal to or greater than the level of concern, then a refined risk assessment is performed to further characterize the risk. A refined assessment takes into consideration more realistic exposure scenarios (such as drift and run-off to non-target habitats) and might consider different toxicity endpoints. Refinements may include further characterization of risk based on exposure modelling, monitoring data, results from field or mesocosm studies, and probabilistic risk assessment methods. Refinements to the risk assessment may continue until the risk is adequately characterized or no further refinements are possible.

4.2.1 Risks to Terrestrial Organisms

A summary of terrestrial toxicity data for permethrin is presented in Appendix V, Table 2. For the assessment of risk, toxicity endpoints chosen from the most sensitive species were used as surrogates for the wide range of species that can be potentially exposed following treatment with permethrin. The terrestrial assessment took into account the range of agricultural application rates that are registered for permethrin, taking into consideration that there may be multiple applications of permethrin in a use season.

4.2.1.1 Terrestrial Invertebrates

4.2.1.1.1 Soil dwelling invertebrates

The lowest 14-day LC_{50} for *Eisenia foetida* is 22.1 mg a.i./kg soil. Taking into consideration the uncertainty factor of 0.5, the LC_{50} used in the risk assessment is 11.05 mg a.i./kg soil. At the highest cumulative application rate (140 g a.i./ha × 6 applications at 7 day intervals), the calculated EEC in soil is 0.307 mg a.i./kg soil. The associated risk quotient based on the maximum application rate (RQ = 0.03), indicates that permethrin is not expected to pose an acute risk to earthworms. No chronic studies were available to conduct a chronic risk assessment for earthworms.

4.2.1.1.2 Honey bees

Screening Level Risk Assessment

Pollinators can be exposed to permethrin from contact and/or feeding on contaminated parts of plants, for example, pollen and nectar. In-hive bees, including immature bees, can be exposed via contaminated plant materials brought back by foraging bees. For the Tier I risk assessment for foliar application, the lowest single spray application rate was used to estimate the EEC. The most sensitive 48-h endpoints for acute contact and oral toxicity tests were used in the risk assessment (0.024 and 0.13 g a.i./bee, respectively).

Contact exposure (expressed as µg a.i./bee) was estimated by multiplying the application rate in kg a.i./ha by 2.4 µg a.i./bee per kg a.i /ha. The estimated residue per bee following the minimum single application of 35 g a.i./ha is 0.084 µg a.i./bee, respectively. The RQs for bees resulting from acute contact exposure to permethrin exceeded the LOC of 0.4 (RQ = 3.5).

Dietary exposure (in µg a.i./bee) was estimated by multiplying the application rate in kg a.i./ha by a conversion factor of 29 µg a.i./bee per kg a.i/ha. The estimated dietary exposure was calculated to be 1.02 µg a.i./bee. The RQs for bees resulting from acute oral exposure exceeded the LOC of 0.4 (RQ = 7.8).

As the lowest single application rate was used, the LOC would also be exceeded for all other application rates for both acute oral and contact exposure.

Higher Tier Risk Assessment

Higher tier field studies with end-use products containing permethrin indicate that there were no significant effects on mortality, foraging ability or brood health at application rates up to 70 g a.i./ha when application occurred prior to bees actively foraging. A cumulative application rate of 220 g a.i./ha (4-6 applications/year at 37 g a.i./ha) also had no significant effect on bee mortality following application over a 3 year study period. There is some evidence to suggest that permethrin may exert a repellent effect on foraging activity immediately following application bees were seen hovering over corn plants while collecting pollen but would not land). Subsequent foraging activity did not appear to be affected.

Most Canadian application rates are higher than those used in the higher tier studies. Therefore where rates are higher, there may be potential risk to pollinators. PMRA is proposing that applications to crops that are at rates greater than those tested and which are highly attractive to pollinators, be prohibited during the bloom period. For crops that are less attractive to pollinators or within the rates tested in higher tier studies, applications will be restricted to the evening when bees are not actively foraging.

4.2.1.1.3 Beneficial arthropods

A quantitative risk assessment could not be conducted for beneficial arthropods because the studies reviewed did not report endpoints (i.e. LR_{50} values).

Acute 5-d contact studies indicate 100% mortality at application rates of 224.2 g a.i./ha and 17 to 85% mortality at 112.1 g a.i./ha for two species of parasitic wasps. Mortalities in other parasitic wasp species ranged from 40-90% at 224.2 g a.i./ha and 0 to 55% at 112 g a.i./ha. Significant reductions in numbers of Hemipteran predators were observed at all application rates tested ranging from 56-224.2 g a.i./ha as well as in Carabidae at 50 g a.i./ha. Significant reduction in abundance of spiders was observed for four weeks post-spraying at a rate of 50 g a.i./ha. No effects were observed in various other arthropod species that were tested at these same application rates.

Proposed minimum single application rates in Canada range from 35-425 g a.i./ha (PMRA 2401443). Considering the effects observed in laboratory and field studies at rates as low as 50 g a.i./ha (spiders, 4-weeks reduction in abundance) beneficial arthropods are expected to be at risk from exposure to permethrin at almost all proposed application rates. Label statements are proposed to warn users of potential affects to beneficial arthropods and to indicate that drift to off-field areas should be minimized.

4.2.1.1.4 Terrestrial Plants

Non-target plants may be exposed to permethrin by direct overspray and spray drift. In a vegetative vigour test, the most sensitive species for which a reduction in biomass was observed, was the monocot *Allium cepa* (onion) at an application rate of 6875 g a.i./ha (effects were <20%). The maximum proposed single application rate in Canada is 425 g a.i./ha. The RQ for terrestrial plants resulting from overspray was calculated as 0.06, indicating that terrestrial plants are not at risk from direct overspray of permethrin. Because no effects were observed due to direct overspray, a risk assessment considering the impact of spray drift of permethrin to terrestrial plants is not required.

At application rates of 1.0 and 8.0 kg a.i./ha, treated plants (two moncotyledon and two dicotyledon species) showed no phytotoxic effects when permethrin was applied directly to seed prior to growth or postemergence at the 2-5 leaf stage of emerged seedlings. Considering that the maximum proposed single application rate is 425 g a.i./ha, this further supports that permethrin use is not expected to result in risk to either seedling emergence or post-emerged terrestrial vascular plants.

4.2.1.1.5 Terrestrial Vertebrates

Foliar applications

For the bird and mammal risk assessment, the ingestion of food items contaminated by spray droplets is considered to be the main route of exposure. The risk assessment is thus based on the estimated daily exposure which takes into account the expected concentration of permethrin on various food items immediately after the last application and the food ingestion rate of different sizes of birds and mammals. At the screening level, only the most conservative exposure estimates are used; i.e., the single highest application rate for agricultural uses (pears at 425 g a.i./ha).

Screening level risk quotients (RQ) are shown in Appendix V, Table 3. For mammals, the LOC is not exceeded for either acute or reproductive effects. For birds, the LOC is exceeded on a reproductive basis for small and medium insectivores and for large birds feeding on short grass (RQ = 2.5 – 4.9) and no acute risk is evident (RQ<1).

To further characterize the reproductive risk to birds, the assessment was expanded to include a range of permethrin residue concentrations on all relevant food items at the lowest single minimum and highest cumulative crop application rates (brassica and leafy vegetables: 34.56 g a.i./ha, and pears: 425 g a.i./ha, respectively). The risk associated with the consumption of food items contaminated from spray drift off the treated field was assessed taking into consideration the projected spray drift deposition of spray quality of ASAE fine for ground application to brassica and leafy vegetables (11%) and ASAE fine for airblast application to pears (74% drift) at 1 m downwind from the site of application.

The reproductive risk to birds feeding on terrestrial food sources, characterized based on maximum and mean residue values, is presented in Appendix V, Tables 4a and 4b.

At the highest single application rate (pears), the LOC for reproductive effects is exceeded for all sizes of birds in all feeding guilds based on maximum residue values on-field and off-field (RQ = 1.1 to 4.9), except medium-sized frugivores and large insectivores feeding off-field (RQ = 0.8 to 0.9). Using mean residue values in food the LOC is only exceeded for small and medium insectivores both on-field and off-field (RQs = 1.95 to 3.38). All other feeding guilds in all size classes do not show a reproductive risk using mean residue values in food items (RQs = 0.36 to 0.88).

At the lowest single minimum agricultural application rate (brassica and leafy vegetables – 34.56 g a.i./ha) permethrin is not expected to pose a reproductive risk to birds.

A reproductive risk was identified for avian species at the highest registered application rate in Canada; however, this risk is considered to be low for the following reasons: 1) the level of concern is only slightly exceeded; 2) it is unlikely that the food items of concern would comprise 100% of the diet of birds and 3) the next highest single application rate is half of the pear rate, therefore, risk will be even lower.

Although the risk to birds is considered to be low, a label statement is required to inform the user of the potential hazard.

4.2.2. Risks to Aquatic Organisms

A summary of aquatic toxicity data for permethrin is presented in Appendix V, Tables 5 to 11. Toxicity information for the transformation products of permethirn is limited and available for freshwater invertebrates and fish. Freshwater invertebrates and fish are shown to be far less sensitive to transformation products (for example, 3-PBA and DCVA) than to parent permethrin. As invertebrates and fish demonstrate the greatest sensitivity to permethrin, the risk assessment is based solely on toxicity and exposure to permethrin.

Screening Level Assessment

To assess the potential for effects from exposure to permethrin, screening level EECs in the aquatic environment were based on a direct application to water. This assessment identifies the taxonomic groups at risk. The calculated EECs were those determined in 15 cm body of water for amphibians and 80 cm body of water for all other aquatic organisms, at the highest cumulative application rate for agricultural uses[5] (140 g a.i./ha × 6 applications at 7 day intervals) registered for use on fruiting vegetables (crop group 8: tomatoes). For the screening level risk assessment for aquatic organisms, the laboratory endpoints were adjusted using factors to account for differences in species sensitivity and protection goals (for example, community, population and individual).

Sufficient acute toxicity data was available for some aquatic taxa to determine HC_5 values (the 5th percentile of the species sensitivity distribution (SSD) for the LC_{50} at 50% confidence intervals). A species sensitivity distribution (SSD) was determined for non-target freshwater

[5] Note: Application rate chosen for aquatic risk assessment differs from that used in other parts of assessment (for example, bird and mammals risk assessment) because the use of the aquatic whole system DT_{50} (43 days) produces the largest cumulative rate for crop group 8: tomatoes.

invertebrates and freshwater fish, estuarine marine invertebrates and fish based on the available data. The hazardous concentration to five percent of species (HC_5) was calculated from the LC_{50} values, using the software program ETX 2.1. The HC_5 is the concentration which is theoretically protective for 95% of species. At the HC_5 exposure level, five percent of all species may be exposed to a concentration which exceeds their LC_{50} toxicity value. The variability around the fraction of species affected (FA value) is indicated by the lower and upper confidence limits (90% CI), which indicates the minimum and maximum percent of species that may be affected at the HC_5 value.

A summary of the SSD analysis is available in Appendix VII; a summary of the aquatic HC_5 values determined follows. The data used to determine the SSDs are found in Appendix VII, Tables 2.1 to Table 2.4.

Freshwater invertebrate HC_5 value: A total of 25 acute toxicity endpoints for freshwater invertebrate species were used for SSD analysis. The median HC_5 value for permethrin for acute effects on freshwater invertebrates was determined to be 0.019 µg a.i./L (CI: 0.0043 to 0.057 µg a.i./L). The variability around the fraction of species affected (FA, expressed as a percentage of all species) indicates a range of 1.5-12.9%. Therefore, exposure to the median HC_5 value (0.019 µg a.i./L) could result in adverse effects in a minimum of 1.5% of species and up to a maximum of 12.9% of all species at the EC_{50} level. This variability indicates that the 95% of species protection level may not always be achieved.

Freshwater fish HC_5 value: A total of 30 acute toxicity endpoints for freshwater fish species were available for SSD analysis. The median HC_5 value of permethrin for acute effects on freshwater fish was determined to be 1.2 µg a.i./L (90% CI: 0.66 to 1.9 µg a.i./L). The variability around the fraction of species affected (FA, expressed as a percentage of all species) indicates a range of 1.7 to 11.7% (90% CI). Therefore, exposure to the median HC_5 value (1.2 µg a.i./L) could result in adverse effects in a minimum of 1.7% of species and up to a maximum of 11.7% of all species at the EC_{50} level. This variability indicates that the 95% of species protection level may not always be achieved.

Estuarine/marine invertebrate HC_5 value: A total of 11 acute toxicity endpoints for estuarine/marine invertebrate species were available for SSD analysis. The median HC_5 value of permethrin for acute effects on estuarine/marine invertebrates was determined to be 0.002 µg a.i./L (90% CI: 0.00003 to 0.0237 µg a.i./L). The variability around the fraction of species affected (FA, expressed as a percentage of all species) indicates a range of 0.7 to 18.9% (90% CI). Therefore, exposure to the median HC_5 value (0.002 µg a.i./L) could result in adverse effects in a minimum of 0.7% of species and up to a maximum of 18.9% of all species at the EC_{50} level. This variability indicates that the 95% of species protection level may not always be achieved.

Estuarine/marine fish HC_5 value: A total of 10 acute toxicity endpoints for estuarine/marine fish species were available for SSD analysis. The median HC_5 value of permethrin for acute effects on estuarine marine fish was determined to be 2.38 µg a.i./L (90% CI: 0.77 to 4.4 µg a.i./L). The variability around the fraction of species affected (FA, expressed as a percentage of all species) indicates a range of 0.6 to 20% (90% CI).

Therefore, exposure to the median HC_5 value (2.38 µg a.i./L) could result in adverse effects in a minimum of 0.6% of species and up to a maximum of 20% of all species at the EC_{50} level. This variability indicates that the 95% of species protection level may not always be achieved.

For the chronic risk assessment the most sensitive NOECs for the various biotic groups were used: freshwater invertebrates, NOEC of 0.0047 µg a.i./L for reproductive effects on *Daphnia magna*; freshwater fish, NOEC = 0.3 µg a.i./L for reproductive effects in fathead minnows; marine invertebrates, NOEC = 0.011µg a.i./L based on mortality; and marine fish, NOEC = 0.83 µg a.i./L based on reduced fry survival. A chronic endpoint for amphibians was not available; therefore, the NOEC = 0.3 µg a.i./L for reproductive effects (based on the chronic fish endpoint) was used.

Toxicity endpoints for most aquatic species were several orders of magnitude lower than the screening level EECs. The risk quotients greatly exceed the level of concern (RQ = 2.4 - 40350) for acute and chronic effects for all aquatic species. Therefore, further refinement of the aquatic risk assessment was required. The calculated risk quotients are summarized in Appendix V, Table 12.

Refined Risk Assessment

The risk to aquatic organisms was refined by taking into consideration the concentrations of permethrin that could be deposited in off-field aquatic habitats that are downwind and directly adjacent to the treated field through spray drift as well as via run-off.

Assessment of Potential Risk from Spray Drift

Spray drift data was used to determine the maximum spray deposit into an aquatic habitat located 1 meter downwind from a treated field. Review of the labels for permethrin-containing end-use products indicate that the end-use products are applied by a variety of application methods. The maximum amount of spray that is expected to drift 1m downwind from the application site during spraying using field sprayer and aerial application methods is determined based on a fine spray droplet size: field sprayer – 11%, aerial – 26%, respectively. The maximum amount of spray that is expected to drift 1m downwind from the application site during spraying using airblast application is 74% and 59% for early and late application, respectively. Given the variation in percent drift off site for each of the application methods, the assessment of potential risk from drift was assessed for the minimum single ground application for brassica and leafy vegetables (34.56 g a.i./ha) and the cumulative maximum airblast application rate for grapes (4 applications of 138 g a.i./ha, at 7-day intervals[6]); these application rates cover the full range of application rates and application methods. The aquatic EEC for the highest cumulative application rate has been revised by adjusting the sum of the applications for dissipation between applications using the DT_{50} value of 43 days (longest of two aquatic whole system half-lives).

The risk quotients indicate that the LOC is exceeded for all organisms and all application methods on an acute and chronic basis (RQs = 1.6 to 21700; Appendix V, Table 13), with the exception of algae (freshwater and marine), freshwater fish for acute effects and marine/estuarine

[6] Different from the screening because grape application is airblast (74% drift) and results in higher EEC from drift compared to direct application used in screening (ground boom application to tomatoes: 11% drift).

fish for acute and chronic effects at the lowest field sprayer single application rate (RQ = 0.02 to 0.57). In order to reduce the potential risk to aquatic species due to drift, buffer zones are required.

Initial spray buffer zones calculated based on fine ASAE spray quality were large and did not fully mitigate the risk to aquatic organisms for some agricultural ground applications and all aerial applications. Therefore spray buffer zones were refined by setting restrictions on various spray application parameters (spray droplet size, wind speed, humidity, temperature, low drift spray nozzle technology, reduced number of applications). Restrictions for aerial applications include spray droplet size (medium/coarse), wind speeds at the time of application (< 10 km/hr), temperature at the time of application (<20°C) and relative humidity at the time of application (<50%). For all ground field sprayer use restrictions include the use of low drift air induction nozzles only, and wind speeds at the time of application (< 8 km/hr). With these restrictions in place the risk to aquatic biota was acceptable.

Assessment of Potential Risk from Runoff

The Surface Water Concentration Calculator (SWCC) model was used to predict estimated environmental concentrations (EECs) resulting from runoff of permethrin following application. The models were run at the lowest single rate (to assess risk at the lowest possible use rate) and the highest rate (to cap the highest risk possible): the lowest maximum single rate is for use on vegetables (69.12 g a.i./ha) and the highest maximum cumulative rate is for use on tomatoes (6 applications of 140 g a.i./ha, at 7-day intervals), respectively. The Level 1 permethrin EECs in a 1-ha receiving water body (15 and 80 cm deep) predicted by SWCC for these crops applications are presented in Appendix V, Table 14. The values reported by SWCC are 90th percentile concentrations of the concentrations determined at a number of time-frames including the yearly peak, 96-hr, 21-d, 60-d, 90-d and yearly average. The EECs used for calculation of the RQs were the highest values at the appropriate depth and appropriate time-frame. Acute and chronic RQ values were calculated using an EEC for the time frame which most closely matched the exposure time used to generate the endpoint (e.g. a 96 hour LC_{50} would use the 96 hour value generated by the model; a 21 day NOEC would use the 21 day EEC value). The acute and chronic RQ values for aquatic organisms are reported in Appendix V, Table 15.

The RQs derived for acute exposure to runoff exceed the LOC for all aquatic organisms at all permethrin application rates (RQ = 1.9 – 2300), except for freshwater and marine/estuarine algae; acute exposure to runoff does not exceed the LOC for freshwater and marine/estuarine fish at the lowest application rate. The RQs derived for chronic exposure indicate that the LOC is exceeded for all aquatic organisms (1.8 - 113), except for freshwater fish and amphibians at the lowest application rate and marine/estuarine fish at all application rates. Mandatory vegetative filter strips are being proposed to reduce movement of permethrin into aquatic habitats.

Water Monitoring

A summary of permethrin monitoring data in surface water bodies relevant to the aquatic risk assessment is presented in Appendix VI. Although permethrin has high use and an extensive use pattern, the review of available Canadian and American surface water and groundwater monitoring data reveals few detections of permethrin in the samples analyzed (3,469 out of

66,042 samples – 5.3% detection). Water monitoring data, particularly for surface water, may miss peak concentrations, as sampling is typically sporadic and peak concentrations can be flushed through a system in a short amount of time after a runoff event. Ancillary data regarding site and timing of application versus the sampling location is not available for the monitoring studies considered in this assessment. Consequently, it is possible that sampling occurred in areas where, or at times, when the pesticide was not used.

Permethrin was detected in 79 of the 2,600 water samples collected across Canada. For aquatic risk assessment purposes, the highest concentration of permethrin detected in surface water (5.04 µg/L) from a sample in New Brunswick, is considered for the acute risk assessment. Using this value, the level of concern for acute effects is exceeded for all freshwater aquatic organisms (RQs range from 4.2 to 265, except for freshwater algae where the RQ is 0.81; Appendix V, Table 16). No monitoring data for marine/estuarine environments were available to assess risks for marine/estuarine organisms.

The available Canadian water monitoring data are not robust enough to fully characterize the risks to aquatic invertebrates because 2405 of 2600 samples (93%) of the samples collected and analyzed for permethrin had limits of detection (LODs) that were higher than the toxicity endpoint for aquatic invertebrates (HC_5= 0.019 µg/L). The analytical methods were not sensitive enough to capture detections of permethrin in water that could potential be a concern to aquatic invertebrates. However, using a conservative approach of using the LOD as an exposure concentration the potential risk quotients (RQs) calculated from these various studies range from 1.6-26.3 for permethrin

Of the 195 samples with a LOD sensitive enough to detect permethrin below the LOC for aquatic invertebrates, 25 (13%) exceeded the toxicity endpoint for aquatic invertebrates of 0.019 µg a.i./L (1% overall samples, or 32% of detections). Sensitivity of the LOD was not a concern in comparison to the freshwater fish and amphibians endpoints (i.e., 0% and 2% of samples had LOD higher than the toxicity endpoints, respectively). Three of the 79 samples with detections in Canada exceeded the endpoint for fish of 1.2 µg a.i./L (0.1% of overall samples, or 4% of the detections), and 9 of them exceeded the endpoint for amphibians of 0.2 µg a.i./L (0.3% of overall samples, or 12% of the detections). Despite the low frequency of detection in water, as well as the insensitivity of some analytical detection limits, there are instances where concentrations were above the toxicity endpoints for aquatic organisms. It is not possible to reliably estimate how often these occur because the toxicity endpoint is below the limit of detection for the majority the samples.

The surface water EECs determined from the aquatic modelling ecoscenario (Appendix V, Table 14) are very similar to the concentrations of permethrin detected in surface water monitoring. The results of the two risk assessments conducted with modelled and monitored concentrations in water support the conclusion that an acute risk to aquatic organisms exists.

Due to the low detection frequency of permethrin in water samples and the small number of samples that were analyzed with a limit of detection low enough to detect concentrations at the level of concern for chronic risk to invertebrates, it is difficult to estimate a long term exposure concentration based on available water monitoring data; a chronic aquatic exposure assessment based on monitoring data, therefore, cannot be conducted.

4.2.3 Use of Vegetative Filter Strips for Reducing Run-off to Aquatic Habitats

To reduce movement of permethrin into aquatic habitats via run-off, PMRA is proposing that vegetative filter strips be mandatory in areas of use.

Since 2008, the USEPA has required statements on all pyrethroid agricultural product labels requiring a 3.05 m (10 ft) vegetative filter strip (VFS) composed of grass or other permanent vegetation between the field edge and aquatic habitats. No fish kill incidents have been reported in the United States since the implementation of these requirements. The absence of further incidences in relation to adherence/implementation of the VFS is uncertain, however, VFSs have been shown to reduce movement of contaminants, excess nutrients, soil and other detrimental components into aquatic systems.

In 2000, the province of Prince Edward Island (PEI) introduced buffer legislation which mandated vegetative filter strips for various land uses, including agricultural crops. The legislation required all agricultural fields that border water courses to maintain a 10-meter vegetated filter strip along the water edge. The minimum buffer width was increased to 15 m in a 2008 amendment to PEI's Environmental Protection Act. Fields with steeper slopes (i.e. > 5%) within 50 meters of the upland boundary of the 10-meter buffer and having no other mitigating management practices in place are required to have a 20-m vegetative filter strip.

The EU has also adopted the use of VFS for sustainable use of pesticides. EFSA has proposed 20 metre VFSs for a number of crop protection products.

5.0 Incident Reports

Since 26 April 2007, registrants have been required by law to report incidents, including adverse effects to health and the environment, to PMRA within a set timeframe. Information on the reporting of incidents can be found on the Pesticides and Pest Management portion of the Canada.ca website.

5.1 Human and Animal Incident Reports excluding spot-on flea and tick products

As of 5 April 2017, incident reports submitted to the PMRA included 142 human, 330 domestic animal, 4 environmental, and 2 packaging failures that involved permethrin.

Incident reports are evaluated by the PMRA to determine whether the reported effects could be related to the pesticide exposure. Of the human incidents that were considered to be possibly associated with the reported exposure to permethrin, there was one serious incident that occurred in the United States. The individual's pre-existing respiratory problems were aggravated after inhaling a dust product. In the remaining incidents, the most commonly reported symptoms were mild gastrointestinal symptoms (such as nausea), respiratory effects (such as coughing, irritated throat), general symptoms (such as headache) or dermal effects (such as rash). Exposure generally occurred following accidental contact with a permethrin product during or shortly after the application of the product. Respiratory and dermal exposures were most frequently reported.

Most products involved in the human incidents were household insecticide sprays. Residential exposure was the most frequently reported scenario. Incidents were typically attributed to applicator or bystander exposure.

Similar trends were observed in the California Department of Pesticide Regulation's Pesticide Illness/Injury Query database and the United States Environmental Protection Agency (USEPA) databases, in which incidents typically occurred following bystander or accidental exposures in non-agricultural settings.

No serious health risks were identified in the incident report data. However the incident information does support the improvement of product labels regarding application, re-entry, and ventilation statements. Further label improvements that would be supported by the incident information include listing potential effects in humans following respiratory or dermal contact, and a statement to indicate that animals should not be permitted in treated areas. Label statements are being proposed to address the concerns identified in the Occupational Exposure risk assessment (Appendix IX).

For the domestic animal incidents considered in this review, cats and dogs were generally exposed to domestic class sprays that were used in or around the home. Accidental ingestion and contact with a treated area were frequently reported as reasons for exposure. Other animals involved in Canadian incidents included cows and horses that were treated directly with a permethrin product.

5.2 Environmental Incident Reports

As of 28 April 2016, four environmental incidents involving permethrin have been submitted to the PMRA. One incident involved bee mortality shortly after application of a permethrin product to elm trees; several dead bumblebees and honey bees were noted on walkways in the vicinity of the sprayed trees (honey bee hives were unaffected). Bumble bees were reported as actively foraging prior to product application. No details are provided as to how the product was applied or the severity of the incident (number of dead bees). Two incidents involved plant damage and in one incident, a squirrel died after an outdoor spray was applied to a lawn; insufficient information is available to establish whether these incidents were the result of permethrin use.

As of 5 October 2015, the USEPA had received fifty-two permethrin-related incident reports. The most frequently reported sites affected were aquatic (mostly fish), plants, and bees. While in some cases, the incidents are confirmed as the result of a registered use, the legality of the majority of incidents (product misuse versus registered use) is undetermined. The information in the incidents is consistent with the known toxicity hazard of permethrin to terrestrial and aquatic organisms. Exposure often occurred as a result of drift or runoff, or direct treatment; this is consistent with the results of the drift and runoff risk assessment.

Twenty-seven incidents report fish kills of which twelve were the result of registered use in agricultural (for example, corn, tomato) or residential areas (around home, lawn, building); the certainty of permethrin as the cause of these incidents ranges from possible to highly probable.

Six of the incidents resulting from registered use report the total number of fish killed which ranges from 17 to 4000 fish per incident. All fish kill incidents reported in the EIIS database occurred prior to the USEPA's mandated label change to permethrin products in 2008 requiring a vegetative filter strip of 10 feet between the site of application and adjacent water bodies.

Eleven incidents report damage to terrestrial plants (in both agricultural and residential settings) of which two were the result of registered use; damage to 142 acres of alfalfa and 72 acres of cauliflower reported after permethrin application is listed as possible and unlikely, respectively.

Of the remaining 14 incidents reports, three are reported as the result of registered use.

Two of these incidents involved the death of butterflies after ultra low volume (ULV) application for mosquito control (1000–10,000 monarch butterflies – highly probable; adult and caterpillar mortality in a colony maintained by a butterfly hobbiest - possible). In an incident involving crayfish mortality in a creek located near a home treated with termiticide, permethrin was listed as highly probable as the cause of mortality. Other incidents included bee mortality or the death of animals (for example, 1 dog, 4 parakeets, 3 birds); these incidents were either the result of misuse or lacked information to ascertain legality of use.

6.0 Value

Permethrin has one of the broadest use patterns for the synthetic pyrethroids and is registered commercially to control major pests on agricultural crops and livestock. It contributes to resistance management by helping to delay the development of resistance when used in rotation with other insecticides with different modes of action. In mushroom production, permethrin is registered to control adult sciarid flies, which can be a major pest in mushroom houses. Pest control in mushroom production consists of sanitation/disinfectant practices, use of insect growth regulators cyromazine and s-methoprene to target sciarid larvae, and conventional insecticides to target adult sciarid flies. Permethrin products are used by pest control operators to target bedbugs and fleas in residential settings in current Integrated Pest Management strategies. Besides other pyrethroids and pyrethrins, there are few other active ingredients registered for use in dwellings for use on fleas (such as boracic acid, d-limonene, s-methoprene, pyriproxyfen, silicon dioxide and thyme and wintergreen oil) and bedbugs (such as diatomaceous earth, silica dioxide, and liquid carbon dioxide).

Domestic products containing permethrin are registered for use on a broad spectrum of pests, such as ants, cockroaches and fleas. Permethrin products are of benefit to homeowners to use with other control methods, such as prevention and non-chemical treatments, in the management of pests in and around homes. Various types of domestic permethrin products are used to control fleas, ticks, mosquitoes and lice on dogs.

7.0 Pest Control Product Policy Considerations

7.1 Toxic Substances Management Policy Considerations

The Toxic Substances Management Policy (TSMP) is a federal government policy developed to provide direction on the management of substances of concern that are released into the environment. The TSMP calls for the virtual elimination of Track 1 substances [those that meet all four criteria outlined in the policy, i.e. persistent (in air, soil, water and/or sediment), bio-accumulative, primarily a result of human activity and toxic as defined by the *Canadian Environmental Protection Act*].

During the review process, permethrin and its transformation products were assessed in accordance with the PMRA Regulatory Directive DIR99-03[7] and evaluated against the Track 1 criteria. The PMRA has reached the following conclusions:

- Permethrin does not meet all Track 1 criteria, and is not considered a Track 1 substance. See Appendix VIII, Table 1 for comparison with Track 1 criteria.
- Permethrin does not form any transformation products that meet all Track 1 criteria.

The use of permethrin is not expected to result in the entry of TSMP Track 1 substances into the environment.

7.2 Formulants and Contaminants of Health or Environmental Concern

During the review process, contaminants in the technical and formulants and contaminants in the end-use products are compared against the *List of Pest control Product Formulants and Contaminants of Health or Environmental Concern* maintained in the *Canada Gazette*.[8] The list is used as described in the PMRA Notice of Intent NOI2005-01[9] and is based on existing policies and regulations including: DIR99-03; and DIR2006-02,[10] and taking into consideration the Ozone-depleting Substance Regulations, 1998, of the *Canadian Environmental Protection Act* (substances designated under the Montreal Protocol). The PMRA has reached the following conclusions:

- Based on the manufacturing process used, impurities of human health or environmental concern as identified in the Canada Gazette, Part II, Vol. 142, No. 13, SI/2008-67 (2008-06-25), including TSMP Track 1 substances, are not expected to be present in the permethrin products.

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7 DIR99-03, *The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy*

8 *Canada Gazette*, Part II, Volume 139, Number 24, SI/2005-114 (2005-11-30) pages 2641–2643; *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern* and in the order amending this list in the *Canada Gazette*, Part II, Volume 142, Number 13, SI/2008-67 (2008-06-25) pages 1611-1613, *Part 1 Formulants of Health or Environmental Concern, Part 2 Formulants of Health or Environmental Concern that are Allergens Known to Cause Anaphylactic-Type Reactions and Part 3 Contaminants of Health or Environmental Concern.*

9 NOI2005-01, *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern under the New Pest Control Products Act.*

10 DIR2006-02, *Formulants Policy and Implementation Guidance Document.*

- Permethrin end-use products do not contain any formulants or contaminants of health or environmental concern identified in the *Canada Gazette*.

8.0 Organisation for Economic Co-operation and Development Status of Permethrin

Canada is part of the Organisation for Economic Co-operation and Development (OECD), which groups member countries and provides a forum in which governments can work together to share experiences and seek solutions to common problems.

As part of the re-evaluation of an active ingredient, the PMRA takes into consideration recent developments and new information on the status of an active ingredient in other jurisdictions, including OECD member countries. In particular, decisions by an OECD member country to prohibit all uses of an active ingredient for health or environmental reasons are considered for relevance to the Canadian situation.

Permethrin is currently acceptable for use in other OECD member countries, including Australia, Europe, and the United States. As of 20 March 2017, no decision by an OECD member country to prohibit all uses of permethrin for health or environmental reasons has been identified.

9.0 Proposed Re-evaluation Decision

The PMRA is proposing that products containing permethrin for use and sale in Canada are acceptable for continued registration provided that the proposed label amendments described in Appendix IX are implemented. Based on the evaluation of currently available scientific information, mitigation measures are proposed to further protect human health and the environment, including a mandatory 10 meter vegetative strip for agricultural products. No additional data are being requested at this time.

9.1 Proposed Regulatory Action Related to Human Health

9.1.1 Proposed Mitigation Related to Toxicology

Label statements are required (see Appendix IX).

9.1.2 Proposed Mitigation Related to Dietary Exposure

Label statements are required for agricultural food/feed crop uses, specifying a plant back interval of 60 days for all non-registered agricultural food/feed crops. Also, limits on the number of applications for tomatoes are proposed.

In addition, label updates are required for certain products registered for uses on livestock and livestock housing as some use directions are not specified on several product labels. These label updates would include the supported use directions (application rate, maximum number of applications, minimum re-treat interval, and/or pre-slaughter interval) on product labels, where applicable.

Please refer to Appendix IX.

9.1.3 Proposed Mitigation Related to Occupational and Residential Exposure

Risks of concern were identified for some scenarios. These scenarios require additional mitigation measures, as described below.

9.1.3.1 Proposed Mitigation Measures for Commercial Products

Uses Proposed for Cancellation

Applications in mushroom houses are proposed for cancellation since there were no data available to assess potential postapplication exposure for this scenario.

Label statements are proposed prohibiting application using fogging equipment and hand-held mist blower/airblast equipment since there are no data available to assess exposure when using this application equipment type.

Use Precautions

For treatment of wood using an enclosed linear system, a label statement regarding wood intended for export to Australia is included.

In order to promote best practices, and to minimize human exposure from spray drift or from spray residues resulting from drift due to agricultural use of permethrin, label statements are proposed to prohibit application when there is potential drift to residential areas, to prohibit application using fogging equipment and handheld mist blowers/airblast equipment.

In order to promote best practices and to minimize human exposure from application of permethrin to residential areas label statements are proposed to prohibit indoor broadcast applications, to prohibit entry into treated areas until sprays have dried, to prohibit application to overhead areas in confined spaces without respiratory and eye protection, and to require ventilation of treated areas.

Personal Protective Equipment

For all agricultural permethrin labels, statements are proposed to include baseline PPE. For all mechanically pressurized handgun applications, mosquito abatement truck mounted mist blower and airblast applications, and wood treatment in an enclosed linear system label statements are proposed requiring additional PPE such as coveralls and chemical-resistant hats.

Restricted Entry Intervals

For agricultural permethrin labels, restricted entry intervals longer than the 12 hour minimum are proposed for some crops and activities.

9.1.3.2 Proposed Mitigation Measures for Domestic Products

Uses Proposed for Cancellation

Label statements prohibiting residential application by hand-held mist blower/sprayer and fogger are proposed since there are no data available to assess exposure when using this application equipment type.

Application by solid fogger is proposed for cancellation since, based on available scientific information; it does not meet Health Canada's current standards for human health protection and poses unacceptable risk to human health.

Label statements prohibiting broadcast applications in residential indoor environments are proposed since, based on available scientific information, they do not meet Health Canada's current standards for human health protection and pose unacceptable risks to human health Cancellation of broadcast treatments for residential indoor environments will reduce the overall aggregate exposure, which are at the threshold of acceptability. It is acknowledged that cancellation of these uses may result in the removal of certain pests from the label that would require a broadcast treatment, such as for fleas and ticks.

Use Precautions

In order to promote best practices and to minimize human exposure from application of permethrin to residential areas, label statements are proposed to to prohibit entry into treated areas until sprays have dried, to prohibit application to overhead areas in confined spaces, and require to ventilation of treated areas.

Application Rates

The application rate for lawns and turf is proposed to be limited to the lower registered rate of 0.123 g a.i./m^2.

9.1.4 Residue Definition for Risk Assessment and Enforcement

The residue definition in plant and animal commodities is currently expressed as the parent compound; (3-phenoxyphenyl)methyl 3-(2,2-dichloroethenyl)-2,2-dimethylcyclopropanecarboxylate, for both risk assessment and enforcement purposes.

For enforcement purposes, the residue definition in plant and animal matrices is proposed to remain the same as the current definition.

For risk assessment purposes, the residue definition in plant and animal commodities was revised as "sum of isomers of permethrin for commodities where permethrin is the only major residue; and sum of isomers of permethrin, isomers of DCVA, MPBA and/or 3-PBA for commodities where permethrin and its metabolites are major residues." For the drinking water risk assessment the residue definition "sum of isomers of permethrin, isomers of DCVA, MPBA and 3-PBA" was established.

9.2 Proposed Regulatory Action Related to the Environment

Based on the environmental assessment, risks of concern to the environment have been identified.

Precautionary label statements are proposed for all product labels, including statements warning of toxicity of permethrin to various biota, revised buffer zones and run-off reduction measures to reduce transfer of permethrin from areas of application to adjacent aquatic habitats.

Due to the risks to aquatic organisms from runoff, the PMRA is proposing a requirement for the construction and maintenance of 10 m VFS. The VFS is intended to reduce the potential for run-off containing permethrin from entering aquatic habitats. The proposed measures would be mandatory for all agricultural uses of permethrin in Canada.

The proposed mitigation measures pertinent to the environment are presented in Appendix XIII. No additional environmental data are being requested at this time.

9.3 Additional Data That May Be Submitted

The PMRA will consider additional data submitted during the 90 day consultation period to further refine the health risk assessment.

To address lack of data to assess the health risks of certain uses, data may include the following:

- Information that fully describes the use of products containing permethrin and human activity associated with their use in mushroom houses, and passive dosimetry data or biological monitoring data for fogger application equipment in mushroom houses.
- Passive dosimetry data or biological monitoring data for the application types proposed for cancellation.

It is recommended that registrants interested in submitting additional data during the 90 day consultation period first consult with the PMRA.

10.0 Supporting Documentation

PMRA documents, such as Regulatory Directive DIR2016-04, *Management of Pesticides Re-evaluation Policy*, and DACO tables can be found on the Pesticides and Pest Management portion of Health Canada's website at https://www.canada.ca/en/health-canada/services/consumer-product-safety/pesticides-pest-management.html. The PMRA documents are also available through the Pest Management Information Service. Phone: 1-800-267-6315 within Canada or 1-613-736-3799 outside Canada (long distance charges apply); fax: 613-736-3798; e-mail: pmra.infoserv@hc-sc.gc.ca.

The federal Toxic Substances Management Policy is available through Environment Canada's website at www.ec.gc.ca/toxics.

List of Abbreviations

↑	increased
↓	decreased
µg	microgram(s)
µL	microlitre(s)
♀	females
♂	males
3-PBA	3-phenoxybenzoid acid
a.i.	active ingredient
abs	absolute
ADI	acceptable daily intake
ALP	alkaline phosphatase
ALT	alanine transaminase
APDM	aminopyrine demethylase
ARfD	acute reference dose
ARTF	Agricultural Re-entry Task Force
AST	aspartate aminotransferase
ATPD	area treated per day
AUC	area under the curve
BMDL	benchmark dose, lower confidence limit
BUN	blood urea nitrogen
bw	body weight
bwg	body weight gain
CAF	composite assessment factor
CDC	Centers for Disease Control and Prevention
CFIA	Canadian Food Inspection Agency
cm	centimetre(s)
cm^2	centimetres squared
C_{max}	maximum concentration
CMC	carboxymethylcellulose
DA	dermal absorption
DEEM-FCID	Dietary Exposure Evaluation Model - Food Commodity Intake Database
DFR	dislodgeable foliar residue
DMSO	dimethyl sulfoxide
DNA	deoxyribonucleic acid
DNT	developmental neurotoxicity
DT_{50}	half-life time
ECD	electron capture detector
EC50	Half maximal effective concentration
EEC	estimated environmental concentrations
ER (α, β)	estrogen receptor
ER	endoplasmic reticulum
ErC_{50}	EC_{50} in terms of reduction of growth rate
EyC_{50}	EC_{50} in terms of reduction of yield rate
et al.	and others
EUP	end use product
F_1	first generation

F_2	second generation
fc	food consumption
FOB	Functional Observational Battery
g	gram(s)
GC	gas chromatography
GD	gestation day
GLC	gas-liquid chromatography
GSH	glutathione
ha	hectare(s)
HC_5	hazardous concentration for five percent of the species
Hct	hematocrit
Hgb	hemoglobin
hr(s)	hour(s)
in vivo	performed or taking place in a living organism
iv	intravenous
kg	kilogram(s)
L	litre(s)
LC_{50}	median lethal concentration
LD_{50}	median lethal dose
Log K_{OW}	octanol-water partition coefficient
LOAEL	lowest observed adverse effect level
M/L/A	mixer/loader/applicator
m	metre(s)
m^2	metres squared
MAS	maximum average score
MCH	mean cell hemoglobin
MCV	mean corpuscular volume
mg	milligram(s)
MIS	mean irritation score
mmHg	millimeters of mercury
MOE	margin of exposure
MRL	maximum residue limit
mRNA	messenger RNA
MSD	mass selective detector
n/a	not available
NCE	normochromatic erythrocytes
NCHS	National Center for Health Statistics
ND	not determined
NHANES	National Health and Nutrition Examination Survey
NOAEL	no observed adverse effect level
PCE	polychromatic erythrocytes
PCT	percent crop treated
PDP	Pesticide Data Program
PEG	polyethylene glycol
per se	in itself
pH	potential of hydrogen
PHED	Pesticide Handlers Exposure Database
PMRA	Pest Management Regulatory Agency

PMRA $DT_{50}/90/t_R$	Representative half-life
PND	postnatal day
PPE	personal protective pquipment
ppm	parts per million
PRZM-GW	Pesticide Root Zone Model Groundwater
q_1^*	cancer potentency factor
RBC	red blood cell
REI	restricted-entry interval
rel	relative
RfD	reference dose
ROW	right-of-way
RQ	risk quotient
SER	smooth endoplasmic reticulum
SOP	standard operating procedure
SWCC	Surface Water Concentration Calculator
$T_{1/2}$	half-life
T3	triiodothyronine
T4	thyroxine
TC	transfer co-efficient
TFP acid	3-(2-chloro-3,3,3-trifluoropropenyl)-2,2-dimethylcyclopropane carboxylic acid
TSH	thyroid stimulating hormone
TTR	turf transferable residue
USEPA	United States Environmental Protection Agency
USC	use site category
USDA	United States Department of Agriculture
WBC	white blood cell
wc	water consumption
wk	week
wt	weight

Appendix I Toxicity Profile and Endpoints for Health Risk Assessment

Table 1 Toxicity Profile of permethrin

Effects are known or assumed to occur in both sexes unless otherwise noted; in such cases, sex-specific effects are separated by semi-colons. Organ weight effects reflect both absolute organ weights and relative organ to bodyweights unless otherwise noted. Effects seen above the LOAEL(s) have not been reported in this table for most studies for reasons of brevity.

Study Type/Animal/PMRA #	Study Results
Pharmacokinetic Sprague-Dawley and Wistar Rats 38-43:57-62 cis: trans isomer ratio PMRA # 1403354, 2127251, 2127252, 2127253, 2127254, 2127256, 2127258, 2327220, 2327221, 2327223	Single oral low-dose: Absorption: Rapid uptake with peak levels in blood noted at 1.5-2.5 hrs w/alcohol-labeled permethrin. Acid-labeled permethrin had lower uptake with peak levels noted from 0-10 hrs post-dosing. Levels declined in the 10-24 hr post-dosing period for both radiolabels. Distribution (alcohol-label only): 1 hr post-dosing, the bulk of the radioactivity was present in the stomach and intestines with the remainder of the radioactivity detected in the lungs, kidneys, skin, fat and liver. Most of the radioactivity was still present in the stomach and intestines 24 hrs post-dosing with highest levels found in fat. By 96 hrs post-dosing radioactivity was found in the fat and the liver. Metabolism: The cis- and trans-esters were readily metabolized by ester cleavage, hydroxylation of geminal dimethyl group in the acid or the phenoxy group of the alcohol and by conjugation of the resulting carboxylic acids and phenols. It appeared that at least some of the hydroxylated acids underwent minor degrees of conjugation. A less hydroxylated derivative was formed from the 1 R, trans- dichlorovinyl acid itself than from the 1 R, trans-permethrin, indicating that permethrin was hydroxylated to some extent before hydrolysis. Excretion: For both radiolabels the majority of radioactivity was excreted within the first 48 hrs. After 7 days, 62% of the radioactivity from the ^{14}C-alcohol permethrin was excreted in the urine and 36% in the feces with 1.6% in the expired air; 50% of the radioactivity from the ^{14}C-acid permethrin was excreted in the urine and 49% in the feces.

Study Type/Animal/PMRA #	Study Results
	Single oral high-dose: Distribution: The radioactivity levels in fat and ovaries of female rats with ^{14}C-alcohol permethrin were about 5 times higher than that with ^{14}C-acid permethrin; no other sex differences were apparent. The highest levels of radioactivity 7 days post-dosing were found in fat. Retention of radioactivity at 7 days post-dosing was between 0.3 and 0.8% of the administered dose. Excretion: The major route of excretion was by feces (71-76%) with urinary elimination accounting for only 18-28% of the administered dose 7 days post-dosing. The majority of radioactivity was excreted within 6-24 hrs with no obvious differences noted in excretion patterns between the sexes or between radiolabels. Multiple oral low-doses: Distribution: The level of radioactivity in fat began to plateau 3 wks after the start of dosing and reached maximum values in fat at 5-7 wks resulting in a half-life in fat of 7-18 days (depending on dosage level). Lesser levels were noted in the liver and kidneys. No radioactivity was detected in brain tissue with either radiolabel. Insignificant levels were noted in fat by 7 wks post-dosing and in the liver and kidney by 7 days post-dosing. A change in the cis:trans isomer ratio (↑ cis- and ↓ trans-) in perirenal fat was reflective of the more readily metabolized trans-isomer. Excretion: Elimination was complete by 7 wks post-dosing. Some studies considered supplemental.
Pharmacokinetic Sprague-Dawley rats 25:75 cis:trans isomer ratio PMRA # 2327213, 2327223	Single oral dose: Absorption: The half-life of absorption was 0.91 hrs with peak concentrations attained within 4 hrs. The oral bioavailability was found to be ~60%. T_{max} in plasma was 3.5 hrs. Distribution: Low levels of permethrin were detected in the liver 0.5-48 hrs after dosing while high levels were detected in the brain and sciatic nerve 48 hrs post-dosing. Distribution half-life

Study Type/Animal/PMRA #	Study Results
	was 4.85 hrs. The maximum amount of permethrin detected in most nervous tissue regions studied was significantly higher than the maximum plasma level. Metabolism: The metabolism of permethrin was rapid and degradation products were identified as meta-phenoxybenzylalcohol and meta-phenoxybenzoic acid. Levels of metabolites in liver were much lower than those in plasma and nervous tissue. The concentrations for both degradation compounds in most nervous tissues were generally similar or lower than those found for the parent compound permethrin. One notable exception was the hypothalamus in which the m-phenoxybenzyl alcohol concentrations were, at all times studied, higher than the permethrin values. Excretion: The elimination half-lives of permethrin and metabolites in tissues were in the range of 7-23 hrs. The elimination half-life from the blood was 12.3 hrs.
Pharmacokinetic Sprague-Dawley rats Cis:trans isomer ratio N/S PMRA # 1403343, 1403351, 2127255, 2327215, 2327220, 2327221	

Study Type/Animal/PMRA #	Study Results
	acid sulfate, phenoxybenzoic acid in the free form and its glucuronic acid and glycine conjugates. Four hydroxylated ester derivatives of permethrin were identified in the feces of the rats given ^{14}C alcohol cis-permethrin along with unchanged parent. These hydroxylated metabolites were not present in the feces of rats given ^{14}C-alcohol trans-permethrin, in which the identified metabolites were phenoxybenzyl alcohol, phenoxybenzoic acid and unchanged parent. Excretion: Results 4 or 12 days after oral administration of either radiolabel showed most of the radiocarbon was recovered in the excreta; essentially none was expired in air. Those given the *trans*- isomer excreted 79-82% of the dose in urine and 16-18% in faeces while rats given the cis- isomer excreted 52-54% in urine and 45-47% in faeces. Quantitative differences in excretion profiles suggested greater metabolism of the trans-isomer when compared to the cis-isomer.
Pharmacokinetic Beagle dogs 50:50 cis:trans PMRA # 2127289, 2127290, 2035764, 2327215, 2327220, 2327221	

Study Type/Animal/PMRA #	Study Results
	Single Dermal application: No radioactivity was distinguishable in any tissue from dogs 7 or 14 days after topical application of permethrin isomers. Excretion: Maximum radiocarbon output appeared in excreta 2-3 days after application. Total radioactive recovery (day 7 or 14) was 73-77%. Most was recovered in patches (52-76% of recovered activity) or from excised skin and skin swab (8-36%). Urinary and fecal excretion, collectively accounted for 12-15% regardless of isomer with higher recovery in the urine for all isomers. Some studies considered supplemental.
Pharmacokinetic Albino rabbits Cis:trans isomer ratio N/S PMRA # 2035764	After topical application of cis- or trans-permethrin, no retention of radiocarbon was noted in any tissues 7 days post-dosing. Total radioactive recovery at day 7 was 83% (cis-isomer) and 67% (trans-isomer). Of the recovered radioactivity, 38-58% was found in the patches and 8-17% was found in the excised skin and skin swab. Urinary and fecal excretion collectively accounted for 34% (cis-isomer) or 46% (trans-isomer) with higher recovery in the urine.
Acute Oral Toxicity Mice PMRA # 2021746, 2327220, 2327221, 2327223	Evans (corn oil): 25:75 cis:trans LD_{50} = 2,394/2,690 mg/kg bw (♂/♀) Alderley Park (Lissatan): 40:60 cis:trans LD_{50} > 4,000 mg/kg bw (♀) Japanese Albino (corn oil): 40:60 cis:trans LD_{50} = 650/540 mg/kg bw (♂/♀) CF1 (corn oil): 10:90 cis:trans LD_{50} = 1,700 mg/kg bw 25:75 cis:trans LD_{50} = 960 mg/kg bw 40:60 cis:trans LD_{50} = 650 mg/kg bw 100:0 cis:trans LD_{50} = 230 mg/kg bw
	dd (corn oil): 40:60 cis:trans LD_{50} = 490 mg/kg bw (+)-trans LD_{50} = 3,100/3,200 mg/kg bw (♂/♀) (+)-cis LD_{50} = 107/85 mg/kg bw (♂/♀) (-)-trans LD_{50} > 5,000 mg/kg bw (-)-cis LD_{50} > 5,000 mg/kg bw Signs of toxicity: hypersensitivity, tremors and ataxia.

Study Type/Animal/PMRA #	Study Results
	Some studies considered supplemental.
Acute Oral Toxicity Rats PMRA # 1237289, 2021746, 2045468, 2046351, 2327220, 2327221, 2327222, 2327223	Wistar (corn oil unless stated otherwise): 20:80 cis:trans LD_{50} > 3,000 mg/kg bw (♀) 25:75 cis:trans LD_{50} = 1,479/12,680 mg/kg bw (♂/♀) 25:75 cis:trans LD_{50} = 341 mg/kg bw (8 day old pups) 25:75 cis:trans LD_{50} = 399 mg/kg bw (16 day old pups) 25:75 cis:trans LD_{50} = 471 mg/kg bw (21 day pups) 30:70 cis:trans LD_{50} = 1,703 mg/kg bw (♀) 39:61 cis:trans LD_{50} = 806/814 mg/kg bw (♂/♀) 40:60 cis:trans LD_{50} = 1,200 mg/kg bw 40:60 cis:trans (Lissatan) LD_{50} > 4,000 mg/kg bw 40:60 cis:trans (neat) LD_{50} = 8,900 mg/kg bw 50:50 cis:trans LD_{50} = 1,000 mg/kg bw (♀) 60:40 cis:trans LD_{50} = 466 mg/kg bw (♀) 80:20 cis:trans LD_{50} = 224 mg/kg bw (♀) Sprague-Dawley (corn oil unless stated otherwise): 36:54 cis:trans (Lissatan) LD_{50} = 2,949 mg/kg bw (♂) 40:60 cis:trans LD_{50} > 5,000 mg/kg bw 41:59 cis:trans LD_{50} = 1,000/860 mg/kg bw (♂/♀) 81:19 cis:trans LD_{50} = 370/320 mg/kg bw (♂/♀) Long-Evans(corn oil unless stated otherwise): 25:75 cis:trans LD_{50} = 1,600 mg/kg bw 40:60 cis:trans LD_{50} = 1,200 mg/kg bw 40:60 cis:trans (neat) LD_{50} = 6,000 mg/kg bw Signs of toxicity: urinary incontinence, dehydration, piloerection, hypersensitivity, stains around the nose, upward curvature of the spine, tremors, hyperthermia, irregular breathing and increased breathing rate. Some studies considered supplemental.
Acute Oral Toxicity Duncan Hartley guinea pigs PMRA # 2327220	40:60 cis:trans (Lissatan) LD_{50} > 4,000 mg/kg bw (♂)
Acute Oral Toxicity New Zealand White rabbits PMRA # 2327220	40:60 cis:trans (Lissatan) LD_{50} > 4,000 mg/kg bw (♀) Signs of toxicity: lethargy, slight incoordination, piloerection, increased respiration, hunched posture, slight incoordination and tremors

Study Type/Animal/PMRA #	Study Results
Acute Dermal Toxicity Various species PMRA # 2327220	Japanese Albino mice, Sprague-Dawley rats: 40:60 cis:trans LD_{50} > 2,500 mg/kg bw Wistar rats: 40:60 cis:trans LD_{50} > 4,000 mg/kg bw (♀) Signs of toxicity: tremors New Zealand White rabbits: 40:60 cis:trans LD_{50} >2,000 mg/kg bw
Acute Inhalation Toxicity Wistar rats PMRA # 1237261	Wistar: 39:61cis:trans LC_{50} = 2.30 mg/L Signs of toxicity: splayed gait, tremors, paw flicking, decreased reflexes and decreased activity
Eye Irritation Rabbits PMRA # 1237262, 2327223	New Zealand White: 39:61 and 55:45 cis:trans = minimally irritating
Dermal Irritation Rabbits PMRA # 1237263, 2327223	New Zealand White: 39:61cis:trans = mildly irritating 40:60 and 55:45 cis:trans = minimally irritating
Dermal Sensitization (Maximization test) Guinea pigs PMRA # 1237264, 2127226, 2327222, 2327223	Albino: 25:75 cis:trans (corn oil) = negative Dunkin Hartley: 39:61 cis:trans (corn oil) = sensitizing
10-Day Oral Toxicity CD-1 mice (♀ only) 25:75 cis:trans isomer ratio PMRA # 2327222	1,600 mg/kg bw/day: 3 mortalities (4 hrs after 1st dose), spasms and convulsions (1 hr post-dosing), ↑ liver wt, ↓ RBC and ↑ LDH Supplemental study.
28-Day Dietary Toxicity Alderley Park mice 39:56 cis:trans isomer ratio	280 mg/kg bw/day: ↑ liver wt, pitting of renal cortex and granular spleen; eosinophilia of centrilobular hepatocytes, ↑ relative kidney, heart and thymus wt (♀)

Study Type/Animal/PMRA #	Study Results
PMRA # 2327220, 2327223	Supplemental study.
10-Day Oral Toxicity Wistar rats (♀ only) 25:75 cis:trans isomer ratio PMRA # 2327222	≥200 mg/kg bw/day: ↑ liver wt and AST Supplemental study.
28-Day Dietary Toxicity Wistar rats 40:60 cis:trans isomer ratio PMRA # 2327220	NOAEL = 50 mg/kg bw/day ≥100 mg/kg bw/day: tremors (1st 24 hrs); ↑ liver wt (♀)
30-Day Dietary Toxicity Long-Evans rats 40:60 cis:trans isomer ratio PMRA # 2327223	≥250/280 mg/kg bw/day: slight-moderate tremors, staining of anogenital fur; ↓ bw (♂) Supplemental study.
35-Day Dietary Toxicity Charles River rats 40:60 cis:trans isomer ratio PMRA # 1403361, 2327220, 2327223	NOAEL = 100 mg/kg bw/day 300 mg/kg bw/day: persistent tremors (on day 2), ↓ bwg, ↑ relative liver wt; ↑ prothrombin time and plasma urea levels, ↑ absolute heart wt (♂); ↓ plasma protein levels (♀)
90-Day Dietary Toxicity Wistar rats 25:75 cis:trans isomer ratio PMRA # 2327221, 2327223	NOAEL = 18 mg/kg bw/day ≥54/54 mg/kg bw/day: 1 mortality, ↑ fat content of renal cortex (♂); ↑ pituitary wt (♀) Partial recovery reported 4 weeks post-dosing No treatment-related effect on estrus cyclicity.
90-Day Dietary Toxicity Wistar rats	NOAEL = 54 mg/kg bw/day ≥180/176 mg/kg bw/day: ↑ relative spleen and lung wt (♂); ↑

Study Type/Animal/PMRA #	Study Results
25:75 cis:trans isomer ratio PMRA # 2327221, 2327223	relative liver wt, ↓ relative thyroid and ↓ adrenal gland wt (♀) Partial recovery reported 4 weeks post-treatment No treatment-related effect on estrus cyclicity.
90-Day Dietary Toxicity Long Evans rats 40:60 cis:trans isomer ratio PMRA # 1403362, 2327220	NOAEL = 5 mg/kg bw/day (♀) ≥25 mg/kg bw/day: centrilobular hepatocyte hypertrophy, skeletal muscle atrophy; ↑ liver wt (♂); tremors (2♀ on day 2) (♀)
90-Day Dietary Toxicity Long-Evans rats 55:45 cis:trans isomer ratio PMRA # 2327223	50 mg/kg bw/day: ↑ relative liver wt (♂); ↓ relative liver wt (♀) Supplemental study.
6-Month Dietary Toxicity Sprague-Dawley rats 40:60 cis:trans isomer ratio PMRA # 2127227, 2327220	NOAEL = 93/110 mg/kg/day 186/220 mg/kg bw/day (♂/♀): hypersensitivity and tremors (early stages of study), ↑ liver wt, hypertrophy of liver parenchymal cells with slight fatty changes; ↑ relative kidney wt (♂)
10-Day Oral Toxicity Dutch Ranch rabbits 25:75 cis:trans isomer ratio PMRA # 2327222	≥200 mg/kg bw/day: ↓ bw, hepatic nodules Supplemental study.
14-Day Oral Toxicity Beagle dogs 40:60 cis:trans isomer ratio PMRA # 2327223	No NOAEL established (range-finding) 500 mg/kg bw/day: tremors and ataxia (1st wk) (♂) Supplemental study.
14-Day Oral Toxicity Beagle dogs	There were no treatment-related clinical signs of toxicity, effects on body weight, hematological or clinical chemistry findings at 500 mg/kg bw/day.

Study Type/Animal/PMRA #	Study Results
25:75 cis:trans isomer ratio PMRA # 2327222	Supplemental study.
90-Day Oral Toxicity Beagle dogs 54:46 cis:trans isomer ratio PMRA # 2327223	NOAEL = 5 mg/kg bw/day ≥50 mg/kg bw/day: tremors and muscle twitching; impaired gait, ataxia, involuntary limb movements, uncontrolled barking, panting and salivation (♂)
90-Day Oral Toxicity Beagle dogs 40:60 cis:trans isomer ratio PMRA # 1403363, 2327220, 2327223	NOAEL = 50 mg/kg bw/day 500 mg/kg bw/day: clinical signs of toxicity (tremors, narcosis with nystagmus on one occasion, 1 animal), ↑ liver wt; ↓ blood glucose, ↑ clotting time (♂); ↑ relative thyroid wt, ↓ absolute ovarian wt, ↑ blood glucose (♀)
90-Day Oral Toxicity Beagle dogs 40:60 cis:trans isomer ratio PMRA # 2127232, 2327220	NOAEL = 100 mg/kg bw/day 2,000 mg/kg bw/day: mild tremors (1-2 hrs post-dosing), ↓ plasma glucose, ↑ relative liver wt; ↓ bwg (♀)
26-Week Oral Toxicity Beagle dogs 25:75 cis:trans isomer ratio PMRA # 2327222, 2327223	NOAEL = 50 mg/kg bw/day 250 mg/kg bw/day: ↓ bw and fc (wks 12 and 22), ↓ pH of urine, ↑ lymphocytes and neutrophils
52-Week Oral Toxicity Beagle dogs 35:65 cis:trans isomer ratio PMRA # 1233639, 2327223	NOAEL = 5 mg/kg bw/day ≥100 mg/kg bw/day: ↓ bw, ↑ ALP (♂: from wk 4, ♀: from wk 16), ↓ ALB and total protein levels, ↑ liver wt, enlargement of hepatocytes with cellular swelling, degenerative changes in adrenal glands (swelling and vacuolation of cells in the zona reticularis, focal inflammation in the zona fasciculata); ↑ platelets (♀)
21-Day Dermal Toxicity	Systemic NOAEL = 500 mg/kg bw/day Dermal LOAEL = 50 mg/kg bw/day

Study Type/Animal/PMRA #	Study Results
Wistar rats 38.6:61.4 cis:trans isomer ratio PMRA # 2127229, 2127230, 2127231, 2327215	≥50 mg/kg bw/day: ↑ incidence of irritation of the skin at the application site 500 mg/kg bw/day: ↓ bw (1st 3 days of dosing); ↑ liver wt (♀)
21-Day Dermal Toxicity New Zealand White rabbits 44:56 cis:trans isomer ratio PMRA # 2327223	Moderate irritation of the skin was observed but the reaction was not significantly different from controls by day 18. Mild irritation was present 10 days after exposure, although it improved daily. Supplemental study.
15-Day Inhalation Toxicity Sprague-Dawley rats 25.2:69.5 cis:trans isomer ratio PMRA # 1234945, 2327215	NOAEC = 0.042 mg/L (~11 mg/kg bw/day) 0.583 mg/L: hypersensitivity to noise/touch, less activity, extensive licking behaviour and whole body tremors (during 1st and 2nd exposures, continued post-exposure), rales, poor grooming and crusty brown staining around the nose, ↓ bwg, ↑ liver wt
13-Week Inhalation Toxicity Sprague-Dawley Rats 60:40 cis:trans isomer ratio PMRA # 1233636, 1234946, 2327223	NOAEC = 0.250 mg/L (~65 mg/kg bw/day) 0.500 mg/L: severe tremors and convulsions (1st 2 wks), ↑ relative liver wt, ↓ hexobarbital-induced sleep times; ↑ induction of liver enzymes (♂ from post-exposure study) (♂)
13-Week Inhalation Toxicity Hartley guinea pigs (♂ only) 60:40 cis:trans isomer ratio PMRA # 1233636, 1234946, 2327223	NOAEC = 0.250 mg/L (~40 mg/kg bw/day) 0.500 mg/L: ↓ bw No sensitization reaction was seen in any test animal at any exposure concentration.
13-Week Inhalation	There were no treatment-related effects on clinical signs of

Study Type/Animal/PMRA #	Study Results
Toxicity Beagle dogs 60:40 cis:trans isomer ratio PMRA # 1233636, 1234946, 2327223	toxicity, body weight, hematology, clinical chemistry, organ weights, pathology or plasma cholinesterase activity up to 0.5 mg/L. Pulmonary function was unchanged but there was a trend towards lower pulmonary compliance and higher pulmonary resistance in the exposed dogs. Supplemental study.
91-Week Dietary Carcinogenicity CFLP mice 25:75 cis:trans isomer ratio PMRA # 1234926, 1234927, 1152999, 2327222	≥50 mg/kg bw/day: ↓ margination of cytoplasm of parenchymal cells of the liver (♂) 250 mg/kg bw/day: ↑ absolute kidney wt, cuboidal/columnar metaplasia of the alveolar epithelium; ↑ liver wt, ↑ relative kidney wt (♂); ↓ fc, focal round cell infiltration in stomach glandular mucosa (♀) Neoplastic Findings (% incidence at 0, 10, 50 and 250 mg/kg bw/day, resp.): Combined Pulmonary Adenomas and Adenocarcinomas: ♀: 3.1%, 7.0%, 10.8% and 21.6% (within HC) Equivocal evidence of tumorigenicity in female mice. Supplemental study.
	NOAEL = 27/30 mg/kg bw/day (♂/♀) Main Study: ≥27/30 mg/kg bw/day: ↓ kidney wt, ↓ degree of vacuolation of the proximal tubular epithelium of the kidney (♂)
	≥111/124 mg/kg bw/day: ↓ bwg, ↑ eosinophilia of centrilobular hepatocytes, ↑ proliferation of SER, ↑ number of microbodies and lysosomes in centrilobular hepatocytes, liver hypertrophy; ↓ brain wt (♂) Interim Sacrifice (26 and 52 wks): ≥27/30 mg/kg bw/day: ↑ hepatic APDM activity; ↑ liver wt, ↓ degree of vacuolation of the proximal tubular epithelium of the kidney (♂); ↑ number of hepatic lysosomes (♀) ≥111/124 mg/kg bw/day: ↑ proliferation of SER, ↑ number of hepatic lysosomes, ↑ eosinophilia of centrilobular hepatocytes; ↑ hepatic APDM activity (♂); ↑ mortalities, ↑ liver wt (♀)

Study Type/Animal/PMRA #	Study Results
	Neoplastic Findings (% incidence at 27/30, 111/124 or 287/316 mg/kg bw/day in ♂/♀, resp.): Combined Pulmonary Adenomas and Adenocarcinomas: ♀s: 15.7%, 11.6%, 15.7% and 21.7% Combined Hepatocellular Adenomas and Carcinomas: ♂: 15.9, 14.7%, 13.0% and 23.5% Evidence of tumorigenicity.
2-Year Dietary Carcinogenicity CD-1 mice 40:60 cis:trans isomer ratio PMRA # 2327215, 2327217, 2327223	≥3/3 mg/kg bw/day (♂/♀): yellow staining of anogenital area and abdominal distension, multifocal hepatocytomegaly; ↓ testicular wt (♂); ↑ liver wt, ↑ focal areas of alveolar cell proliferation (♀) Neoplastic Findings (% incidence at 0/0, 3/3, 71/357 or 286/714 mg/kg bw/day in ♂/♀, resp.): Combined Bronchioloalveolar Adenomas and Bronchioloalveolar Carcinomas: ♀: 21.1%, 35.3%*, 51.5%** and 63.8%** [HC 13.5% (6.5-22.4%)] Combined Hepatocellular Adenomas and Hepatocellular Carcinomas: ♂: 32.4%, 45.3%, 53.1%** and 41.7%*; ♀: 9.1%, 11.3%, 39.7%** and 46.2%** [HC: ♂: 14.0% (5.3-20.0%); ♀: 4.3% (1.1-11.0%)] Evidence of tumorigenicity in male and female mice. Supplemental as chronic toxicity study.

Study Type/Animal/PMRA #	Study Results
100-Week Dietary Carcinogenicity CD-1 mice (♀ only) Cis:trans isomer ratio N/S Non-guideline PMRA # 2327215	780-807 mg/kg bw/day: slightly ↓ bwg (treated for 65 or 78 wks and allowed to recover to wk 101), slightly ↓ fc and ↓ fe, ↑ absolute liver wt, hepatic centrilobular hypertrophy, karyomegaly and kupffer cell hypertrophy (recovery noted for all durations), inflammatory liver changes, amyloid deposits and eosinophilic foci, ↑ specific activity of CYP4A, ↑ total enzyme activities per liver of CYP, CYP1A, CYP2B, CYP2E1 and CYP3A2 and ↑ total enzyme activity per liver of CYP4A, clara cell hyperplasia in the lungs of all treated animals (↓ during recovery). Neoplastic effects (in 0 and 780-807 mg/k bw/day ♀ resp.): Bronchioloalveolar Adenomas: 39 wks: 8.0% vs. 18.0%, 52 wks: 10.2% vs. 32.6%**, 65 wks: 8.0% vs. 30.4%** and 78 wks: 10.4% vs. 42.3%**. The lung adenomas did not occur any earlier in the treated animals than in the control groups. An increase was also noted in animals allowed to recover (recovery up to 78 wks: 10.4%, 30.6%**, 42.4%** and 50.0%** in control, and animals exposed for 39, 52 and 65 wks, resp.; recovery up to 101 wks: 14.0%, 42.7%**, 46.7%**, 48.9%** and 48.5%** in control and animals exposed for 39, 52, 65 and 78 wks, resp.). There was no increase in lung carcinomas. Basophilic Hepatocellular Adenomas: ↑ incidence for 39, 52 or 78 wks followed by recovery (7-10% compared to 1% in controls Eosinophilic Hepatocellular Adenomas: ↑ incidence after 78 wks of exposure to permethrin and after the recovery period (10% compared to 1-2% in controls). No increase in hepatocellular carcinoma incidence was seen and the time to tumour onset for the adenomas was unaffected. Evidence of tumorigenicity in female mice.
104-Week Dietary Chronic Toxicity/Carcinogenicity Wistar rats 25:75 cis:trans isomer ratio PMRA # 2327215, 2327222	NOAEL = 10 mg/kg bw/day ≥50 mg/kg bw/day: focal disturbances in the growth pattern of thyroid follicular cells; periacinar hypertrophy of hepatocytes, hepatocyte fatty vacuolation, ↑ mortalities (after 94 wks) (♂) Neoplastic Findings (% incidence at 0, 10, 50 and 250 mg/kg bw/day, resp): Thyroid Follicular Cell Adenomas: ♀: 0.0%, 7.5%, 0.0% and

Study Type/Animal/PMRA #	Study Results
	15.0%. Evidence of tumorigenicity in female rats.
104-Week Dietary Chronic Toxicity/Carcinogenicity Wistar rats 40:60 cis:trans isomer ratio PMRA # 2127235, 2127236, 2327215, 2327220, 2327223	NOAEL = 19/40 mg/kg bw/day in ♂/♀, resp. Main Study: ≥19 mg/kg bw/day : yellow staining of genital fur, hypertrophy of centrilobular hepatocytes; ↑ liver wt, ↑ relative kidney wt, ↑ hepatic APDM (♂) ≥37/40 mg/kg bw/day : ↑ proliferation of SER; animals died earlier than those at lower dose levels, ↑ pituitary wt (♂); ↑ liver wt, ↑ hepatic APDM, hypertrophy of centrilobular hepatocytes (♀) Interim Sacrifice (52 wks): ≥19 mg/kg bw/day : ↑ proliferation of SER; ↑ hepatic APDM activity (♂); hepatocyte vacuolation and ↑ absolute liver wt (♀) ≥37/40 mg/kg bw/day : lipid vacuolation; ↓ kaolin-cephalin index and prothrombin index (♂); ↑ hepatic APDM activity, ↓ absolute kidney wt (♀) No evidence of carcinogenicity.
24-Month Dietary Chronic Toxicity/Carcinogenicity Long-Evans rats 40:60 cis:trans isomer ratio PMRA # 2327220, 2327223	NOAEL = 5 mg/kg bw/day Main study: 25 mg/kg bw/day: ↑ glucose levels, ↑ absolute liver wt; ↓ clotting time (♂); tremors (2♀, study day 2), ↓ bw, ↑ absolute ovarian wt, distended uterus/uterine horns (♀) Interim Sacrifice: 25 mg/kg bw/day: ↓ WBC and ↑ hgb (♂); ↑ glucose levels (18 months), ↓ clotting time (12 months) (♀) Unacceptable for evaluation of carcinogenic potential.
In vivo, Medium-term Bioassay for Screening Carcinogens F344 rats (♂ only) 25:75 and 39:61 cis:trans isomer ratios	Without diethylnitrosamine initiation, permethrin did not induce GST-P positive liver cell foci. However, with diethylnitrosamine initiation, permethrin had significantly ↑ number of GST-P positive hepatic foci per unit area.

Study Type/Animal/PMRA #	Study Results
PMRA # 2078457	
Dominant Lethal 40:60 cis:trans isomer ratio PMRA # 2327215, 2327220	Negative in CD-1 mice.
Dominant Lethal 25:75 cis:trans isomer ratio PMRA # 2327223	Negative in CD-1 mice (Supplemental Study)
Micronucleus Cis:trans isomer ratio N/S PMRA # 2127250, 2327215	Negative in CD-1 mice (Supplemental Study).
Micronucleus Cis:trans isomer ratio N/S PMRA # 1073896	Equivocal in Swiss albino mice (Supplemental Study).
Chromosome Aberration 40.3:59.7 cis:trans isomer ratio PMRA # 2127248, 2127249	Negative in bone marrow of Wistar rats.
Chromosomal Aberration Cis:trans isomer ratio N/S PMRA # 1073895	Negative in Swiss albino mice (Supplemental study).
Sex-linked Recessive Lethal 45:55 cis:trans isomer ratio PMRA # 2327223	Negative in Drosophila melanogaster (Supplemental study).
Host-mediated 40:60 cis:trans isomer ratio	Negative with Salmonella typhimurium G46/mice (Supplemental study)

Study Type/Animal/PMRA #	Study Results
PMRA # 2327220	
Host-mediated 40:60 cis:trans isomer ratio PMRA # 2327221	Negative (Supplemental study).
Ames (reverse mutation) 38-44.7:52-61.4 cis:trans isomer ratio PMRA # 1237268, 2127247, 1403348, 2327215, 2327220, 2327221, 2327223	Negative in 10 studies using Salmonella typhimurium and Escherichia coli (Some studies considered supplemental).
Mitotic gene conversion 38:52 cis:trans isomer ratio PMRA # 2327223	Negative in Saccharomyces cerevisiae D4.
Differential Toxicity 38:52 cis:trans isomer ratio PMRA # 2327223	Negative in Esherichia coli and Bacillus subtilis.
Unscheduled DNA Synthesis Cis:trans isomer ratio N/S PMRA # 1223389, 2327215	Negative in primary rat hepatocytes (Supplemental study).
Unscheduled DNA Synthesis 38:52 cis:trans isomer ratio PMRA # 2327223	Negative in primary rat hepatocytes.
Gene Mutation Cis:trans isomer ratio N/S PMRA # 2327223	Negative in Chinese hamster lung V79 cells (Supplemental study).
Chromosomal Aberration	Positive without activation, equivocal with activation in

Study Type/Animal/PMRA #	Study Results
Cis:trans isomer ratio N/S PMRA # 2327223	Chinese hamster ovary cells (Supplemental study).
Sister Chromatid Exchange Cis:trans isomer ratio N/S PMRA # 2327223	Positive without activation, equivocal with activation in human lymphocytes (Supplemental study).
Micronucleus Cis:trans isomer ratio N/S PMRA # 2327223	Positive without activation, equivocal with activation in human lymphocytes (Supplemental study).
Micronucleus Cis:trans isomer ratio N/S PMRA # 2327223	Equivocal without activation in human lymphoctes (Supplemental study).
Chromosomal Aberration Cis:trans isomer ratio N/S PMRA # 2327223	Positive without activation, equivocal with activation in human lymphocytes (Supplemental study).
3-Generation Dietary Reproduction Toxicity Wistar rats 25:75 cis:trans isomer ratio PMRA # 2327220, 2327223	Parental, offspring and reproductive NOAELs = 180 mg/kg bw/day Parental, Reproduction and Offspring: No treatment-related signs of toxicity.
3-Generation Dietary Reproduction Toxicity Long-Evans rats 40:60 cis:trans isomer ratio PMRA # 2327220, 2327223	Parental, Reproduction and Offspring: No treatment-related signs of toxicity up to 6.7 mg/kg bw/day. Supplemental study.
3-Generation Dietary Reproduction Toxicity	Parental and reproductive NOAELs = 67 mg/kg bw/day Offspring NOAEL = 33 mg/kg bw/day

Study Type/Animal/PMRA #	Study Results
Wistar rats 40:60 cis:trans isomer ratio PMRA # 2127237, 2127238, 2127243, 2327215, 2327223	Parental (F_0, F_1 & F_2): 170 mg/kg bw/day: whole body tremors (all generations), ↓ body weight gain (during pre-mating period only), ↑ food consumption (♂: during pre-mating period, ♀: throughout). Reproduction (F_0, F_1 & F_2): 170 mg/kg bw/day: ↓ mean pup weight Offspring (F_1, F_2 & F_3): 67 mg/kg bw/day: ↑ incidence of buphthalmos (F_{2a}, F_{2b}, F_{3a} and F_{3b}) 170 mg/kg bw/day: whole body tremors (F_{2a}), ↑ incidence of buphthalmos (F_{1b}, F_{2a}, F_{2b}, F_{3a} and F_{3b}), cystitis-pyelonephritis (F_{1a}, $F1_b$, F_{3b})
Developmental Toxicity CD rats 37.5:57.8 cis:trans isomer ratio PMRA # 2327220, 2327223	Maternal and developmental NOAELs = 225 mg/kg bw/day Maternal and Developmental: No treatment-related signs of toxicity
Developmental Toxicity Wistar rats 38:62 cis:trans isomer ratio PMRA # 1237266, 1237267, 2327215	Maternal and developmental NOAELs = 50 mg/kg bw/day Maternal: 150 mg/kg bw/day: tremors, head flicking, piloerection, ↓ bwg and fc during dosing interval Developmental: 150 mg/kg bw/day: ↑ incidence of thickened mid-point of the 10th rib, ↑ incidence of unossified odontoid, centrum of 2nd cervical vertebra and calcaneum, μ short length of 14th extra rib

Study Type/Animal/PMRA #	Study Results
Developmental Toxicity Dutch Belted rabbits 40:60 cis:trans isomer ratio PMRA # 1237269, 1237270, 2127244, 2127245, 2127246, 2327215, 2327223	Maternal LOAEL = 600 mg/kg bw/day Developmental NOAEL = 600 mg/kg bw/day Maternal: ≥600 mg/kg bw/day: animals sacrificed moribund or found dead with little or no feces produced and excess fur in the stomach, little or no feces or urine noted on at least one occasion Developmental: ≥1,200 mg/kg bw/day: ↑ number of early and late post-implantation losses, ↑ in post-implantation loss per litter, ↓ number of live fetuses per litter, ↓ ossification of the forelimbs and hindlimbs, ↑ incidence of skeletal variants, ↑ unossified sternebra and ↑ anteriorly moved articulation of the pelvic girdle, major malformations (2 fetuses), ↑ partially ossified pubis of pelvis
3-Week Oral Reproductive Toxicity During Puberty ICR mice (♂ only) Cis- and trans-permethrin PMRA # 2350515	(+)-cis permethrin: ≥25 mg/kg bw/day: ↓ peripheral and testicular benzodiazepine receptor (PBR) and 17β-hydroxysteroid dehydrogenase (17β-HSD) mRNA levels, ↓ testicular HMG-CoA synthase and P450sec mRNA levels, down-regulated testicular StAR mRNA levels (-)-cis permethrin: ≥25 mg/kg bw/day: ↓ testicular HMG-CoA synthase (+)-trans permethrin: ≥25 mg/kg bw/day: ↓ testicular HMG-CoA synthase mRNA levels (-)-trans permethrin: ≥25 mg/kg bw/day: ↓ testicular HMG-CoA synthase and P450sec mRNA levels, down-regulated testicular StAR mRNA levels
6-Week Oral Sperm Motility and Morphology ICR mice (♂ only) Cis-permethrin PMRA # 2078463	

Study Type/Animal/PMRA #	Study Results
	testosterone concentrations, ↑ plasma LH levels, down-regulation of HMG-CoA reductase mRNA expression level, slightly ↓ levels of scavenger receptor class B type 1 and low-density lipoprotein receptor mRNA, severely ↓ mRNA levels for StAR, suppressed P450scc mRNA expression in the testes, ↑ incidence of a few abnormal seminiferous tubules with vacuoles or lack of germ cells, slightly ↑ incidence of damage to the mitochondria of the Leydig cells, cis-permethrin residues in the testes
6-Week Oral Sperm Motility and Morphology ICR mice (♂ only) Cis- and trans- permethrin PMRA # 2078462	No treatment-related effect noted in clinical signs of toxicity and weights of reproductive organs Cis-permethrin: 70 mg/kg bw/day: ↓ caudal epididymal sperm count and motility, ↓ intratesticular and plasma testosterone levels, markedly inhibited PBR and StAR mRNA expression levels in the testes, ↓ P450scc mRNA expression in the testes, ↑ incidence of abnormal seminiferous tubules with vacuoles Trans-permethrin: No effect on the caudal epididymal sperm count and motility, the intratesticular and plasma testosterone levels, the level of PBR and StAR mRNA expression and P450scc mRNA expression in the testes or on seminiferous tubule morphology. 70 mg/kg bw/day: ↑ levels of testicular and urinary 3-PBA as compared to the cis-permethrin exposed group (3 and 7-fold higher)
In vitro, Sperm Motility Sprague-Dawley rats (♂ only) Cis:trans isomer ratio N/S PMRA # 2077605	≥16 µmol/L: ↓ straight-line velocity and linearity after 1 and 2 hrs of incubation, ↓ curvilinear velocity after 4 hrs
8-Week Dietary Sperm Motility and Morphology Lewis rats (♂ only) Cis:trans isomer ratio N/S PMRA # 2077604	No treatment-related effect noted on body weight, absolute and relative weights of the testes and epididymides, relative sperm production, number of sperm in the caput/corpus, sperm transit time in the caput/corpus, sperm morphology throughout the study, plasma levels of follicle-stimulating hormone or histopathology of the testes and epididymis 25 mg/kg bw/day: slightly ↓ number of mature spermatids in the testis, slightly ↓ daily sperm production, ↓ number of

Study Type/Animal/PMRA #	Study Results
	sperm in the cauda epidiymis, slightly ↓ sperm transit time in the cauda and slightly ↓ levels of testosterone and luteinizing hormone Supplemental study.
Androgenic/Anti-androgenic Activity: Hershberger Assay Estrogenic Activity: Uterine gene expression and Uterotrophic Assays Sprague-Dawley rats 24.8:71.8 cis:trans isomer ratio PMRA # 2078467, 2340850	In the Hershberger assay, permethrin did not affect the androgen-dependent tissue weights in castrated male rats at dose levels up to 100 mg/kg bw/day whereas testosterone propionate induced ↑ weights of androgen-dependent sex accessory tissues. The administration of permethrin orally to testosterone propionate-treated castrated male rats led to ↓ in androgen-dependent sex accessory tissue weights at 10, 50 and 100 mg/kg bw/day. In the Calbindin D9k gene expression assay, the level of uterine CaBP-9k mRNA was induced in response to permethrin as well as co-administration of permethrin with 17 β-Estradiol. In the Uterotrophic assay, subcutaneous treatment with permethrin ↑ uterine wet weights and enhanced 17 β-Estradiol-induced uterine wet weights at all doses tested; maximal increases were seen at 200 and 800 mg/kg bw permethrin. ↑ uterine weights by permethrin were inhibited by co-administration of IC 182,780. Permethrin had estrogen-like effects on female rats and anti-androgenic effects on male rats.
Androgenic/Anti-androgenic Activity: Hershberger Assay Sprague-Dawley rats (♂ only) Cis:trans isomer ratio N/S PMRA # 2324694, 2340850	The weight of the ventral prostrate and seminal vesicles was significantly reduced at 50 mg/kg of permethrin when co-administered with testosterone propionate compared to testosterone propionate alone, demonstrating weak anti-androgenicity. Supplemental study.
Androgenic/Anti-androgenic Activity: Hershberger Assay Estrogenic activity: Uterotrophic Assay	In the Hershberger Assay, no significant changes noted in any of the sex accessory tissues of the permethrin-exposed groups (25, 50 and 75 mg/kg bw/day) whereas animals exposed to testosterone propionate had ↑ weights of all sex accessory tissues.

Study Type/Animal/PMRA #	Study Results
Sprague-Dawley rats Cis:trans isomer ratio N/S PMRA # 2350517, 2340850	In the Uterotrophic Assay, permethrin did not cause an ↑ in uterine weights at any dose level (37.5, 75 and 150 mg/kg bw/day)compared to positive controls
In vitro Reporter Gene - African monkey kidney cell line (CV-1 cells) transfected with pSV-Gal reporter Cis:trans isomer ratio N/S PMRA # 2350527, 2340850	Permethrin was a weak anti-androgen. No androgen agonism was detected. Supplemental study.
Androgen Receptor and Human Estrogen Receptor Binding 21.8:75.5 to 73:24 cis:trans isomer ratio PMRA # 2350525, 2340850	Recombinant Yeast Screening Assay: Permethrin had very weak estrogenic (agonist) activity (10^7 to 10^8 less than estradiol); 2/4 sources showed no estrogenic activity. Permethrin had anti-androgenic (antagonist) activity (10^2 less than flutamide). Metabolites: Cyclopropane permethrin acid had anti-estrogenic activity (200-fold less than tamoxifen) 3-phenoxybenzoic acid had anti-estrogenic activity (20-fold less than tamoxifen) 3-phenoxybenzyl alcohol had weak estrogenic activity (10^5 less than estradiol) and anti-androgenic activity (5-fold less than flutamide) Permethrin at 73:24 cis:trans isomer ratio showed no estrogenic activity.
Cell Proliferation and Competitive Binding Cis:trans isomer ratio N/S PMRA # 2350508, 2340850	Permethrin produced an estrogen receptor specific agonist response at 10^{-10} to 10^{-7}M. Supplemental study.
Cell Proliferation and pS2 mRNA Expression Assays - MCF-7 Human Breast Carcinoma Cell Line	Permethrin induced pS2 mRNA expression and cell proliferation at 100 µM.

Study Type/Animal/PMRA #	Study Results
Cis:trans isomer ratio N/S PMRA # 2350512, 2340850	Supplemental study.
Transcriptional Activation, Yeast Two-Hybrid and Estrogen Receptor Binding Cis:trans isomer ratio N/S PMRA # 2350523, 2340850	Permethrin did not show any estrogenic or anti-estrogenic effects at the tested concentrations in any of the assays. Supplemental study.
Transcriptional Activation - MDA-kb2 cells Cis:trans isomer ratio N/S PMRA # 2324694, 2340850	Permethrin was an androgen antagonist, inhibiting the activity of dihydrotestosterone at 10^{-5} M. Supplemental study.
Cell Proliferation, pS2 and ERα mRNA Expression - MCF-7 human breast carcinoma cell line Cis:trans isomer ratio N/S PMRA # 2350514	Permethrin and PBCOH exhibited partially estrogenic responses at 10^{-6} -10^{-7} mol/L in these assays.
Acute Oral Neurotoxicity Sprague-Dawley rats 50:50 cis:trans isomer ratio PMRA # 2127239, 2127240, 2327215, 2327223	300 mg/kg bw: tremors, staggered gait, splayed hindlimbs, exaggerated hindlimb flexion and hypersensitivity to sound (2 days post-dosing, recovery noted by day 3), alterations during functional observation battery testing (whole body tremors, staggered gait, splayed hindlimbs, abnormal posture while moving, exaggerated hindlimb flexion and convulsions on the first day of functional and behavioural testing), ↓ forelimb grip strength, ↑ auditory response, uncoordinated landing; 1 mortality (day 0) (♀) Supplemental study.
13-Week Dietary Neurotoxicity Sprague-Dawley rats 40:60 cis:trans isomer ratio	NOAEL = 15.5/18.7 mg/kg bw/day (♂/♀) No effects on motor activity or neuropathology. ≥92/111 mg/kg bw/day: splayed hindlimbs, staggered/impaired gait, ↑ landing foot splay, ↓ grip strength

Study Type/Animal/PMRA #	Study Results
PMRA # 2127242, 2327214, 2327215	and whole-body tremors, abnormal posture during movement; ↑ changes in fecal boli (♂)
4-Week Oral Behavioral Assessment of F_1 animals ICR (CD-1) mice 40:60 cis:trans isomer ratio Non-guideline PMRA # 2045466, 2046351	Parental and offspring NOAELs = 4.9 mg/kg bw/day Parental: ≥9.8 mg/kg bw/day: tremors, salivation, hyperactivity and liquid feces (3-5 hrs post-dosing, during the dosing phase of the study), ↓ bw and bwg (during gestation and lactation) Offspring: No treatment-related effect on external abnormalities, the development of physical features, pinna detachment, primary coat of down hair, incisor eruption, development of fur, eye or ear opening, testes descent or vaginal opening ≥9.8 mg/kg bw/day: ↓ number of live pups, ↓ bw and bwg (throughout), ↓ surface righting ability (PNDs 3, 4, 5, 6 and 7), ↑ time to develop the negative geotaxis reflex (PNDs 10 and 15), ↓ cliff avoidance reflex (PNDS 4, 6, 8 and 10), ↑ tendency to swim in circles (PNDs 6, 8, 10 and 12) and slower to develop the ability to raise head higher with age when swimming (PNDs 6, 10 and 14), ↓ open field activity (PNDs 14 and 21), ↓ time spent in social interaction (PND 30)
Acute Oral Neurotoxicity Long-Evans rats 50:50 cis:trans isomer ratio PMRA # 2078468, 2327214, 2327223	NOAEL = 25 mg/kg bw ≥75 mg/kg bw: ↓ activity counts, ↑ excitability and aggressive behaviour, abnormal motor movement/tremors (all at 4 hrs post-dosing), ↓ grip strength for hindlimb and ↑ reactivity to a click stimulus (recovery noted by 24 hrs); ↓ grip strength for forelimb, altered motor activity and difficulty in removal from cage (recovery by 24 hrs) and ↑ body temperature (♂)
Acute Dietary Neurotoxicity Wistar rats 90:10, 40:60 and 25:75 cis:trans isomer ratios PMRA # 2327214	Mortality and clinical signs of neurotoxicity (tremors, hypersensitivity) with 300 mg/kg bw of 25:75, 40:60 and 90:10 cis:trans isomer ratios (greatest with the 90:10 cis:trans isomer ratio). Supplemental study.

Study Type/Animal/PMRA #	Study Results
Acute Oral Neurotoxicity Long-Evans rats Cis:trans isomer ratio N/S PMRA # 2078469, 2078470	≥30 mg/kg bw: ↑ in auditory startle response amplitude Lethality (LD_{50}) results: Neonatal (PND 11): 254 (181-322) mg/kg bw Weanling (PND 21): 201 (131-299) mg/kg bw Adult (PND 72): 406 (100-524) mg/kg bw Supplemental study.
Acute Oral Neurotoxicity Sprague-Dawley rats (♂ only) Cis:trans isomer ratio N/S PMRA # 2078454	≥200 mg/kg bw: rearing, clonic convulsions (head/body twitches), whole body convulsions, slight-moderate tremors, hunched body, slight gait impairment, more energetic response to approach and touch (recovery within 24 hrs) Supplemental study.
Acute Oral Motor Activity Long-Evans rats (♂ only) 40:60 cis:trans isomer ratio PMRA # 2078450	$BMDL_{20}$ of 22.95 mg/kg bw for motor activity.
Acute Oral Behavioral Long-Evans rats (♂ only) Cis:trans isomer ratio N/S PMRA # 2045464	≥50 mg/kg bw: ↑ acoustic startle response amplitude Supplemental study.
8-Day Dietary Neurotoxicity Sprague-Dawley rats 40:60 cis:trans isomer ratio PMRA # 1403329, 1403331, 2327214, 2327215	NOAEL = 160 mg/kg bw/day No treatment related effect on histopathology of the brain or spinal cord. 454 mg/kg bw/day: mortalities (days 5-6) and animals sacrificed (days 7-8), tremors and muscle twitching (starting from day 1), ↓ bwg, disintegration of axons and nodal demyelination of the sciatic nerve, very slight to slight swelling of the sciatic nerve
10-Day Oral Behavioral Assessment of Pups Wistar rats (♂ only)	No treatment-related effect on gross behavioural abnormalities noted throughout the study or onbehavioural activities on PND21. No effect noted in superoxide dismutase activity or in DOPAC (3,4-dihydroxy-phenylacetic acid) levels or on phospholipids.

Study Type/Animal/PMRA #	Study Results
25:75 cis:trans isomer ratio PMRA # 2045465, 2046351	34 mg/kg bw/day: ↑ spontaneous locomotor activity and slightly ↑ rearing and grooming counts (PND35), ↓ striatal dopamine levels (PND35), ↑ HVA concentration, ↓ glutathione levels of striatum cells, ↓ GPx activity in the plasma (PND35), ↑ carbonyl group formation in striatum cells, ↑ oxidation index of erythrocytes and ↓ superoxide anion production in monocytes Supplemental study.
14-Day Dietary Neurotoxicity Wistar rats (♂ only) 40:60 cis:trans isomer ratio PMRA # 2327214, 2327215, 2327220	LOAEL = 125 mg/kg bw (♂) First study: ≥125 mg/kg bw/day: slight-convulsive whole body tremors, hyperactivity and hypersensitivity to noise (1st wk), ↓ bw, bwg and fc, ultrastructural changes in the sciatic nerve, disruption of the myelin sheath, degenerating nerve fragments and vacuolated Schwann cells Second study: ≥150 mg/kg bw/day: whole body tremors, hyperactivity and hypersensitivity to noise, ↓ bw, bwg and fc ≥187.5 mg/kg bw/day: hypertrophy of Schwann cells
14-Day Dietary Neurotoxicity Charles River rats 50:50 cis:trans isomer ratio PMRA # 1403332, 2327220	300 mg/kg bw/day: mortalities (days 1-5,), severe tremors, hindlimb paralysis, hypersensitivity to stimuli and diarrhea, axonal swelling and myelin degeneration in neurons of the sciatic nerve in the animals that were not autolyzed
90-Day Dietary Neurotoxicity Sprague-Dawley rats 40:60 cis:trans isomer ratio PMRA # 1142338, 1166041, 2035762, 2327215	There were no treatment-related microscopic findings in peripheral, sciatic, sural and tibial nerves. ≥200 mg/kg bw/day: intermittent fine tremors (first 2 days), irritability and hyperexcitability (wks 1 to 3) Full recovery of clinical signs at 400 mg/kg bw/day three days post-dosing Supplemental study.

Study Type/Animal/PMRA #	Study Results
Dermal Neurotoxicity Sprague-Dawley rats (♂ only) 55:45 cis:trans isomer ratio PMRA # 1403327, 1403333	LOAEL = 2,500 mg/kg bw/day First study (24-hr exposure): 5,000 mg/kg bw: disintegration of sciatic nerve axons Second study (5-day exposure): ≥2,500 mg/kg bw/day: axonal swelling in sciatic nerves (day 7)
Delayed Neurotoxicity Domestic hens (♀ only) 25:75 to 50:50 cis:trans isomer ratio PMRA # 1403334, 2127260, 2327215, 2327223	Negative for delayed neurotoxicity (3 studies).
Two-month Neurotoxicity Adult Leghorn hens (♀ only) Cis:trans isomer ratio N/S PMRA # 2045474	500 mg/kg bw/day: ↑ incidence of 'minor' neuropathological changes in the spinal cord and the sciatic nerve that consisted of an increase in the frequency of slightly enlarged axons.
In vitro effect on spontaneous glutamate network-dependent activity ICR mice 41:58 cis:trans isomer ratio PMRA # 2077602	Permethrin inhibited spontaneous activity in glutamatergic networks in primary cultures of murine cortical and spinal cord cells; the inhibition was not readily reversible

Study Type/Animal/PMRA #	Study Results
Oral Immunotoxicity BALB/c mice (♀ only) Cis:trans isomer ratio N/S PMRA # 2078465	No treatment-related effect noted on body and spleen weights throughout the study. The ability of splenic lymphocytes to proliferate in response to the T or B cell mitogen was not affected. 0.4 mg/kg bw/day: ↓ unidirectional mixed lymphocyte responses ie. blastogenesis of the splenocytes, ↓ in cytotoxic activity of T lymphocytes, ↓ cytotoxicity produced by natural killer cells Supplemental study.
Acute Dermal Immunotoxicity C57BL/6N mice (♀ only) 42.3:57.7 cis:trans isomer ratio PMRA # 2045463, 2046351	In vitro exposure: ≥25 µM: ↓ splenocyte proliferation after 72 hrs of culture In vivo exposure: ≥440 mg/kg bw: ↓ splenic organ wt ≥660 mg/kg bw: ↓ thymic and splenic cellularity, ↓ thymic organ wt, 1,100 mg/kg bw: inhibition of splenic T cell proliferation
Acute Dermal Immunotoxicity C57BL/6N mice (♀ only) 42.3:57.7 cis:trans isomer ratio PMRA # 2078466	No treatment-related effect on splenic weight and cellularity, thymocyte proliferation and splenic macrophage phagocytic ability throughout the study. 1,100 mg/kg bw: ↓ thymic cellularity and wt, ↓ immune response in isolated splenic leukocytes including splenic T-cell proliferative response to mitogen, splenic macrophage hydrogen peroxide production and splenic B lymphocyte-specific antibody production, ↓ splenocyte proliferation, thymocyte proliferation, tremors and ataxia, ↑ mortality within hrs
Repeat Dose Dermal Immunotoxicity C57BL/6 mice (♀ only) 42.3:57.7 cis:trans isomer ratio PMRA # 2078464	No treatment-related effect on body weight, cellularity of the spleen and bone marrow, expression of thymocyte CD4, CD8 or CD45R, expression of splenic CD45R, Thy 1.2 or Mac-1, expression of bone marrow CD45R and CD45, or on histopathology of the thymus and spleen throughout the study for any exposure pattern. Exposure 1 (every day for 10 consecutive days): ≥66 mg/kg bw/day: ↓ relative thymus and spleen wt and ↓ total number of leukocytic cells in the thymus (cellularity) 2 days post-dosing

Study Type/Animal/PMRA #	Study Results
	Exposure 2 (every other day for 7 exposures): No treatment-related effects noted.
	Exposure 3 (every other day for 14 exposures): 220 mg/kg bw/day: ↓ total number of leukocytic cells in the thymus (cellularity) 2 and 10 days post-dosing Exposure 4 (every day for 30 consecutive days): ≥22 mg/kg bw/day: ↓ total number of leukocytic cells in the thymus (cellularity) 30 days post-dosing (lacked statistical significance) Contact hypersensitivity assay: Inhibition of ear swelling response 2 days post-dosing (≥22 mg/kg bw/day) and 10 and 30 days post-dosing (≥66 mg/kg bw/day) with all dose regimes
4-Week Dietary Hepatotoxicity Wistar rats (♀ only) 36.2:61 cis:trans isomer ratio PMRA # 2327220	125 mg/kg bw/day: slight tremors (1♀ during 1st wk, ↓ bw (normal by 28 days), ↓ fc and fe, ↑ liver wt, ↑ hepatic microsomal aminopyrine-N-demethylase activity, ↑ SER in rat liver cells, ↑ hepatic cytochrome P-450 and slightly ↑ plasma alanine transaminase (wk 2) Impartial recovery of hepatic effects at 8 weeks post-dosing Supplemental study.
26-Week Dietary Hepatotoxicity Wistar rats 40:60 cis:trans isomer ratio PMRA # 2327220, 2327223	≥10 mg/kg bw/day: 1 mortality (wk25), ↓ bw (0 to 2 wks) and bwg, ↑ proliferation of SER in hepatocytes and aminopyrine N-demethylase activity (♂) Supplemental study.
Acute Dermal Paraesthesia Guinea pigs (♀ only) 36:54 cis:trans isomer ratio PMRA # 2045471	Minimal evidence of parasthesia at concentrations of up to 10% (w/v)
16-Day Dermal Irritation New Zealand Albino rabbits	Visual erythema was noted over the initial six applications but did not worsen. Histopathological alterations involved acanthosis, an increase in the number of cell layers of the stratum granulosum and a thickening of the stratum corneum.

Study Type/Animal/PMRA #	Study Results
Cis:trans isomer ratio N/S PMRA # 2045472	Supplemental study.
Analysis of urinary metabolites Humans 25:75 cis:trans isomer ratio PMRA # 2327221, 2327222, 2327223	2 mg technical permethrin: Excreted 18-39% of the administered dose of 2-4 mg as the metabolite 3-(2,2-dichlorovinyl)-2,2-dimethyl-cyclopropane-carboxylic acid in urine collected over 24 hrs. Supplemental study.

Table 2 Toxicology Endpoints for Use in Health Risk Assessment for Permethrin

Exposure Scenario	Study	Point of Departure and Endpoint	CAF[1] or Target MOE
	Acute oral neurotoxicity study - rats	$BMDL_{20}$ of 22.95 mg/kg bw (↓ motor activity)	300
	ARfD = 0.08 mg/kg bw		
	Co-critical toxicity studies: 4-wk oral - mice, 90-day oral - dogs, 52-wk oral - dogs, 2-yr dietary - rats	NOAEL = 5.0 mg/kg bw/day (effects on the liver, body weight and/or clinical signs of neurotoxicity)	300
	ADI = 0.02 mg/kg bw/day		
Short-, Intermediate- and Long-term dermal	21-day dermal toxicity study - rats	NOAEL = 500 mg/kg bw/day (HDT, ↓ bw and adaptive liver effects)	300
Short-, Intermediate- and Long-term inhalation	13-wk inhalation toxicity study - rats	NOAEL = 65 mg/kg bw/day (signs of neurotoxicity)	300
Acute-term aggregate risk assessment	Oral: Acute oral neurotoxicity study - rats Dermal: N/A	Oral: $BMDL_{20}$ of 22.95 mg/kg bw (↓ motor activity) Dermal: N/A Inhalation: N/A	300

Exposure Scenario	Study	Point of Departure and Endpoint	CAF[1] or Target MOE
	Inhalation: N/A		
Short- and Intermediate-term aggregate risk assessment	Oral: 90-day oral toxicity study - rats Dermal: N/A Inhalation: 13-wk inhalation toxicity study - rats	Oral: NOAEL = 5 mg/kg bw/day (tremors) Dermal: N/A Inhalation: NOAEL = 65 mg/kg bw/day (tremors)	300
Long-term aggregate risk assessment	Oral: 52-wk oral toxicity study - dogs Dermal: 21-day dermal toxicity study - rats Inhalation: 13-wk inhalation toxicity study - rats	Oral: NOAEL = 5 mg/kg bw/day (liver toxicity) Dermal: NOAEL = 500 mg/kg bw/day (liver toxicity) Inhalation: NOAEL = 65 mg/kg bw/day (liver toxicity)	300
Cancer	A cancer potency factor of 9.87×10^{-3} $(mg/kg\ bw/day)^{-1}$ was derived based on the combined incidence of lung adenomas and carcinomas in female mice orally treated with permethrin.		

1 CAF (composite assessment factor) refers to a total of uncertainty and *Pest Control Products Act* factors for dietary assessments; MOE refers to a target MOE for occupational and residential assessments.

Appendix II Occupational and Residential Tables

Table 1 Short-, Intermediate-, and Long-term Exposure Estimates and MOEs for Agricultural Occupational Handlers

Crop	Application Equipment [a]	Activity Scenario	Formulation	Application Rate	Area Treated per Day (ha/day) [b]	Dermal Exposure [c] (µg/kg a.i./day)	Inhalation Exposure [d] (µg/kg a.i./day)	Dermal MOE [e]	Inhalation MOE [f]
		ML				108.67	3.40	4600	19000
		A				20.53	0.15	24000	440000
	Airblast	MLA			20	405.92	1.13	1200	57000
	Groundboom Custom	MLA			360	160.88	4.90	3100	13000
	Groundboom Large area	MLA			107	47.82	1.46	10000	45000
	Groundboom Small area	MLA			26	11.62	0.35	43000	180000
	MPHW	MLA				1.64	0.08	300000	830000
	Backpack	MLA				9.45	0.11	53000	600000
	MPHG	MLA			3800 L	245.41	6.63	2000	9800
Fence Rows (tobacco)	ROW	MLA	Liquid	6.36E-04 kg a.i./L	3750 L	27.54	0.20	18000	330000
	MPHW	MLA				1.64	0.08	310000	830000
	Backpack	MLA				9.53	0.11	52000	600000
	MPHG	MLA			3800 L	247.66	6.63	2000	9800
	Automated boom sprayer	MLA		0.15 kg a.i./ha	3	0.29	0.01	1700000	7200000
	MPHW	MLA			150 L	1.65	0.08	300000	820000
	MPHG	MLA			3800 L	246.75	6.67	2000	9700
	Backpack	MLA			150 L	19.61	0.22	26000	290000
	MPGH	MLA			3800 L	509.40	13.77	980	4700
	MPHW	MLA		1.5E-03 kg/animal	470 animals	8.31	0.40	60000	160000
	Back rubber	ML			470 animals	0.39	0.01	1300000	5300000
	Cloth, pour on	MLA			120 animals	102.29	1.45	4900	45000
	Ear tag	A	Slow release		210 animals	NA	NA	NA	NA
	Backpack	MLA			470	47.99	0.55	10000	120000

Crop	Application Equipment [a]	Activity Scenario	Formulation	Application Rate	Area Treated per Day (ha/day) [b]	Dermal Exposure [c] (µg/kg a.i./day)	Inhalation Exposure [d] (µg/kg a.i./day)	Dermal MOE [e]	Inhalation MOE [f]
Sheep				kg/animal	animals				
	MPHG	MLA			470 animals	49.22	1.33	10000	49000
	Aerosol	A	Pressurized product	7.26E-03 kg/animal	120 animals	1596.01	17.92	310	3600
	MPHW	MLA				14.72	0.71	34000	92000
	Backpack	MLA				84.96	0.97	5900	67000
	MPHG	MLA				87.13	2.36	5700	28000
Horses	Aerosol, cloth, pour-on	A	Pressurized product	7.26E-03 kg/animal	26 animals	123.61	1.75	4000	37000

MLA = mixer, loader, applicator; A = applicator; MOE = margin of exposure; MPHW = manually pressurized handwand; MPHG = mechanically pressurized handgun

[a] Unless otherwise specified personal protective equipment includes a single layer (long pants, long-sleeved shirt) and chemical-resistant gloves. Gloves are not worn during aerial application.

[b] Based on default assumptions and Statistics Canada data.

[c] Where dermal exposure = (unit exposure × area treated per day × application rate)/80 kg.

[d] Where inhalation exposure = (unit exposure × area treated per day × application rate)/80 kg.

[e] Based on a short-, intermediate-, long-term dermal NOAEL of 500 mg/kg bw/day and a target MOE of 300. All calculated MOEs exceed or approach the target MOE.

[f] Based on a short-, intermediate-, long-term inhalation NOAEL of 65 mg/kg bw/day and a target MOE of 300. All calculated MOEs exceed the target MOE.

Table 2 Cancer Exposure and Risk Estimates for Agricultural Occupational Handlers

Crop	Application Equipment [a]	Activity Scenario	Application Rate	Area Treated per Day (ha/day) [b]	Work Days per Year [c]	LADD [d] (µg/kg bw/day)	Cancer Risk [e]
		ML				0.0735	7E-07
		A				0.0117	1E-07
	Airblast	MLA		7		0.0980	1E-06
	Groundboom Custom	MLA		240	30	0.6801	7E-06
	Groundboom Large area	MLA		60		0.0227	2E-07
	Groundboom Small area	MLA		12		0.0045	4E-08
	MPHW	MLA				0.0015	2E-08
	Backpack	MLA				0.0070	7E-08
	MPHG	MLA		3800 L		0.2028	2E-06
Fence Rows (tobacco)	ROW	MLA	6.36E-04 kg a.i./L	3750 L	2	0.0098	1E-07
	MPHW	MLA				0.0023	2E-08
	Backpack	MLA				0.0105	1E-07
	MPHG	MLA		3800 L		0.3042	3E-06
	Automated boom sprayer	MLA	1.58 kg a.i./ha	3		0.0004	4E-09

Crop	Application Equipment [a]	Activity Scenario	Application Rate	Area Treated per Day (ha/day) [b]	Work Days per Year [c]	LADD [d] (µg/kg bw/day)	Cancer Risk [e]
Commercial Woodlots	MPHW	MLA	7.0E-05 kg a.i./L	150 L	1	3.9E-04	4E-09
	MPHG	MLA		3800 L		0.0510	5E-07
	Backpack	MLA		150 L		0.036	4E-08
	MPHG	MLA		3800 L		0.1052	1E-06
	MPHW	MLA	1.5E-03 kg a.i./animal			0.0039	4E-08
	Back rubber	ML				0.0002	2E-09
	Cloth, pour on	MLA		120 animals		0.0386	4E-07
	Ear tag	A		210 animals	1	NA	NA
	Backpack	MLA				0.0177	2E-07
	MPHG	MLA				0.0203	2E-07
	Aerosol	A	7.26E-03 kg a.i./animal	120 animals	3	0.8828	9E-06
	MPHW	MLA				0.0069	7E-08
	Backpack	MLA				0.0314	3E-07
	MPHG	MLA				0.0360	4E-07
Horses	Aerosol	A	7.26E-03 kg a.i./animal	26 animals	2	0.0466	5E-07

MLA = mixer, loader, applicator; A = applicator; LADD = Lifetime Average Daily Dose; MPHW = manually pressurized handwand; MPHG = mechanically pressurized handgun

[a] Unless otherwise specified personal protective equipment includes a single layer (long pants, long-sleeved shirt) and chemical-resistant gloves. Gloves are not worn during aerial application.

[b] Based on default assumptions and Statistics Canada data.

[c] Based on the number of applications per year. 30 applications is assumed for custom applicators.

[d] LADD = Absorbed Daily Dose × treatment frequency × working duration/(365 days × 78 years). Treatment frequency = 1 to 6 applications/year for farmers and 30 application per year for custom applicators. Working duration = 40 years. ADD is a sum of exposures from Table IV.1. A dermal absorption value of 12% was included in the dermal component of the ADD

[e] A q_1^* value of 0.00987 (mg/kg bw/day)$^{-1}$ was considered appropriate to use in the cancer risk assessment. Cancer risks in the range of 1×10^{-5} were considered to be acceptable.

Table 3 Commercial Applicator in Residential Areas Exposure and Risk Assessment

Scenario	Formulation	Application Equipment	PPE [a]	Application Rate [b]	ATPD [c]	Dermal Exposure [d] (mg/kg bw/day)	Inhalation Exposure [f] (mg/kg bw/day)	Dermal MOE [e]	Inhalation MOE [g]
		Backpack	Baseline		150 L	0.05	6.01E-04	9500	110000
		MPHG	Coveralls [h]		3800 L	0.60	3.70E-02	830	1800
		MPHW			150 L	9.13E-03	4.37E-04	55000	150000
		Hose-end Sprayer		9.10E-05 kg a.i./m^2	20000 m^2	0.05	9.33E-05	11000	700000
		Backpack			150 L	0.04	4.88E-04	12000	130000
		MPHG	Coveralls [h]		3800 L	0.49	3.01E-02	1000	2200
		MPHW			150 L	0.007	3.56E-04	67000	180000
		Hose-end Sprayer		0.022 kg a.i./L	150 L	0.23	6.23E-03	2200	10000
		Backpack			150 L	0.05	6.01E-04	9500	110000
		MPHW			150 L	0.01	4.37E-04	55000	150000
	Ready-to-use	Aerosol		0.00199 kg a.i./can	14 cans	0.05	5.72E-04	9800	110000
Mosquito Abatement	Liquid	Airblast	CR hat, Baseline	0.1134 kg a.i./ha	1200 ha	0.71	1.54E-02	710	4200
		Backpack			150 L	0.10	1.17E-03	4900	55000
		MPHG			860 L	0.61	1.64E-02	830	4000
		MPHW			150 L	0.02	8.54E-04	28000	76000
		Rod Injector				0.005	1.65E-04	95000	390000
		Sub-slab Injector				0.005	1.65E-04	95000	390000
Wood	Liquid	Spray Box	CR coveralls	0.01 µg/µg/cm^2	NA	1.02E-05	NA [i]	49000000	NA
		Backpack				0.05	5.82E-04	9800	110000
		MPHW				8.84E-03	4.24E-04	57000	150000
	Ready-to-use	Aerosol		0.00053 kg a.i./uniform		0.10	1.08E-03	5200	60000
	Liquid	Dip		0.00732 kg a.i./uniform		4.68E-04	1.46E-05	1100000	4400000

MPHG = mechanically pressurized handgun; MPHW = manually pressurized handwand; PPE = personal protective equipment; ATPD = area treated per day; MOE = margin of exposure; CR = Chemical-resistant.

[a] Baseline = long sleeved shirt, long pants and chemical-resistant gloves. Coveralls = Cotton coveralls over long sleeved shirt, long pants and chemical-resistant gloves.

[b] Maximum application rates were used.

[c] Default area treated per day used when available. Aerosol based on professional judgement and other USEPA risk assessments (piperonyl butoxide) assuming 2 containers/house and a commercial applicator being able to treat 7 houses/day (USEPA, 2006). Treated articles based on data provided by DND.
[d] Where dermal exposure (mg/kg bw/day) = (unit exposure × 0.001 mg/µg × area treated per day × application rate)/80 kg.
[e] MOE = margin of exposure; Dermal MOE = dermal NOAEL/dermal exposure, based on a dermal NOAEL of 500 mg/kg bw/day and a target MOE of 300 applicable to short-, intermediate-, long-term scenarios.
[f] Where inhalation exposure (mg/kg bw/day) = (unit exposure × 0.001 mg/µg × area treated per day × application rate)/80 kg.
[g] MOE = margin of exposure; Inhalation MOE = inhalation NOAEL/inhalation exposure, based on a inhalation NOAEL of 65 mg/kg bw/day and a target MOE of 300 applicable to short-, intermediate-, long-term scenarios. Shaded cells indicate MOEs <300.
[h] Cotton coveralls were required for the cancer risk assessment for this scenario, so the values for the same scenario were shown in this table as well.
[i] Inhalation was considered to be negligible in comparison to dermal exposure for wood treatment, based on the SIG study.

Table 4 Commercial Applicator in Residential Areas Cancer Risk Assessment

Scenario	Formulation	Application Equipment	PPE [a]	ADD [b] (mg/kg bw/day)	LADD [c] (mg/kg bw/day)	Cancer Risk [d]
		Backpack	Baseline	6.92E-03	1.17E-04	1E-06
		MPHG	Coveralls	1.09E-01	1.84E-03	2E-05
		MPHW		1.53E-03	2.58E-05	3E-07
		Hose-end Sprayer		5.82E-03	9.81E-05	1E-06
		Backpack		5.63E-03	9.49E-05	9E-07
		MPHG	Coveralls	8.88E-02	1.50E-03	1E-05
		MPHW		1.25E-03	2.10E-05	2.E-07
		Hose-end Sprayer		3.39E-02	5.71E-04	6E-06
		Backpack		6.92E-03	1.17E-04	1E-06
		MPHW		1.53E-03	2.58E-05	3E-07
	Ready-to-use	Aerosol		6.69E-03	1.13E-04	1E-06
Mosquito Abatement	Liquid	Airblast	CR hat, Baseline	1.00E-01	1.69E-03	2E-05
		Backpack		1.35E-02	2.28E-04	2E-06
		MPHG		8.90E-02	1.50E-03	1E-05
		MPHW		2.99E-03	5.05E-05	5E-07
		Rod Injector		7.98E-04	1.35E-05	1E-07
		Sub-slab Injector		7.98E-04	1.35E-05	1E-07
Wood	Liquid	Spray box	CR apron/ coveralls	1.23E-06	2.20E-08	2E-10
		Backpack		6.71E-03	1.96E-04	2E-06
		MPHW		1.49E-03	4.34E-05	4E-07
	Ready-to-use	Aerosol		1.26E-02	7.10E-05	7E-07
	Liquid	Dip		7.07E-05	3.98E-07	4E-09

MPHG = Mechanically pressurized handgun; MPHW = Manually pressurized handwand; PPE = Personal protective equipment; ATPD = Area treated per day; LADD = Lifetime average daily dose
[a] Baseline = long sleeved shirt, long pants and chemical-resistant gloves. Coveralls = Cotton coveralls over long sleeved shirt, long pants and chemical-resistant gloves.
[b] ADD = (Dermal exposure × Dermal absorption (12%)) + Inhalation exposure. Exposure values from Table IV.3.
[c] LADD = Absorbed Daily Dose × treatment frequency × working duration/(365 days × 78 years). Treatment frequency = 30 applications/year for PCOs and 52 applications/year for aircraft disinsection and 10 days for treated articles. Working duration = 16 years. ADD is a sum of dermal and inhalation exposures from Table IV.3. A dermal absorption value of 12% was included in the dermal

component of the ADD.
[d] A q_1^* value of 0.00987 (mg/kg bw/day)$^{-1}$ was considered appropriate to use in the cancer risk assessment. Cancer risks in the range of 1×10^{-5} were considered to be acceptable. Shaded cells indicate cancer risks > 1×10^{-6}; however, due to conservatisms in the risk assessment, these cancer risks were considered to be acceptable.

Table 5 Non-Cancer Dermal Exposure and Risk Estimates for Occupational Postapplication Activities

Crop	Applications		Activity	TC [c] (cm^2/hr)	DFR [d] (µg/cm^2)	Dermal Exposure [e] (µg/kg bw/day)	MOE [f]	REI [g] (days)
	Per year [a]	Rates [b] (kg a.i./ha)						
			hand weeding, propping, orchard maintenance	100	1.26	12.61	40000	0.5
			transplanting	230	1.26	29.00	17000	0.5
			scouting, hand pruning, training	580	1.26	73.14	6800	0.5
			hand harvesting	1400	1.26	176.55	2800	0.5
			thinning fruit	3000	1.26	378.33	1300	0.5
			hand weeding, hand pruning	70	0.62	4.33	120000	0.5
			scouting	210	0.62	12.98	39000	0.5
			transplanting	230	0.62	14.22	35000	0.5
			hand harvesting, tying/training	1100	0.62	68.00	7400	0.5
			irrigation (hand set)	1750	0.62	108.18	4600	0.5
			hand weeding, thinning plants	70	0.88	6.15	81000	0.5
			scouting	210	0.88	18.44	27000	0.5
			scouting, hand harvesting	1100	0.88	96.60	5200	0.5
			irrigation (hand set)	1750	0.88	153.67	3300	0.5
			hand weeding, thinning plants	70	0.88	6.15	81000	0.5
			scouting	210	0.88	18.44	27000	0.5
			hand harvesting, roguing	1100	0.88	96.60	5200	0.5
			scouting, thinning plants, hand harvesting	1300	0.88	114.16	4000	0.5
			irrigation (hand set)	1750	0.88	153.67	3300	0.5
			hand weeding	4400	0.88	386.38	1300	0.5
			hand weeding	70	0.175	1.23	410000	0.5
			transplanting	230	0.175	4.03	120000	0.5
			scouting, hand harvesting	1100	0.175	19.25	26000	0.5
			irrigation (hand set)	1750	0.175	30.63	16000	0.5
			transplanting	230	0.81	18.61	27000	0.5
			scouting, hand pruning, hand weeding, bird control, frost control,	640	0.81	51.79	9700	0.5

Crop	Applications		Activity	TC [c] (cm^2/hr)	DFR [d] (µg/cm^2)	Dermal Exposure [e] (µg/kg bw/day)	MOE [f]	REI [g] (days)
	Per year [a]	Rates [b] (kg a.i./ha)						
			propagating, trellis repair					
			hand harvesting	1400	0.81	113.30	4400	0.5
			irrigation (hand set)	1750	0.81	141.63	3500	0.5
			tying/training, hand harvesting, leaf pulling	8500	0.81	687.90	730	0.5
			girdling, turning	19300	0.81	1561.93	320	0.5
			transplanting	230	0.88	20.20	25000	0.5
			scouting, thinning plants, hand harvesting, mechanically-assisted harvesting	1300	0.88	114.16	4400	0.5
			irrigation (hand set)	1750	0.88	153.67	3300	0.5
			scouting, topping, tying/training	4000	0.88	351.26	1400	0.5
			hand weeding	4400	0.88	386.38	1300	0.5
			hand harvesting	5150	0.88	452.24	1100	0.5
			hand weeding	70	1.16	8.12	62000	0.5
			scouting, bird control	90	1.16	10.44	48000	0.5
			scouting	210	1.16	24.36	21000	0.5
			scouting	1100	1.16	127.60	3900	0.5
			irrigation (hand set)	1750	1.16	203.01	2500	0.5
			hand detasseling, hand harvest	8800	1.16	1020.84	490	0.5
Greenhouse cucumber, tomato	6	0.15	All activities	1400	2.25	315.00	1600	0.5
			All activities	230	1.26	29.07	17000	0.5
			Irrigation (hand set)	1750	1.26	221.17	2300	0.5
			hand weeding, thinning plants	70	0.88	6.15	81000	0.5
			scouting	210	0.88	18.44	27000	0.5
			transplanting	230	0.88	20.20	25000	0.5
			hand harvesting	1100	0.88	96.60	5200	0.5
			hand harvesting, scouting, thinning plants	1300	0.88	114.16	4400	0.5
			irrigation (hand set)	1750	0.88	153.67	3300	0.5
			hand weeding	4400	0.88	386.38	1300	0.5
			hand weeding, hand pruning	70	0.95	6.65	75000	0.5
			scouting	210	0.95	19.96	25000	0.5

Crop	Applications		Activity	TC [c] (cm^2/hr)	DFR [d] (µg/cm^2)	Dermal Exposure [e] (µg/kg bw/day)	MOE [f]	REI [g] (days)
	Per year [a]	Rates [b] (kg a.i./ha)						
			transplanting	230	0.95	21.87	23000	0.5
			hand harvesting, tying/training	1100	0.95	104.58	4800	0.5
			irrigation (hand set)	1750	0.95	166.37	3000	0.5
			hand weeding, scouting	90	0.58	5.19	96000	0.5
			transplanting	230	0.58	13.27	38000	0.5
			hand harvesting, mechanically-assisted harvesting, canopy management	800	0.58	46.16	11000	0.5
			irrigation (hand set)	1750	0.58	100.97	5000	0.5
			hand weeding	100	0.18	1.75	290000	0.5
			transplanting	230	0.18	4.03	120000	0.5
			hand pruning, scouting	580	0.18	10.15	49000	0.5
			seed cone harvest	1400	0.18	24.50	20000	0.5
			irrigation (hand set)	1750	0.18	30.63	16000	0.5
			seeding production harvest	6700	0.18	117.25	4300	0.5

TC = transfer coefficient; DFR = dislodgeable foliar residue; MOE = margin of exposure; REI = restricted entry interval

[a] The label listed maximum number of applications per year.

[b] The label listed maximum application rates.

[c] Transfer coefficients are from ARTF (2008).

[d] Based on dislodgeable foliar residue data on day 0 using the minimum interval between applications.

[e] Dermal Exposure = DFR × TC × 8 hr/80 kg.

[f] Based on the short-, intermediate-, long-term dermal NOAEL of 500 mg/kg bw/day and a target MOE of 300. Shaded cells indicate MOEs < 300.

[g] Restricted entry interval = day at which the dermal exposure results in an MOE = 300.

Table 6 Cancer Risk Estimates for Occupational Postapplication Activities

Crop	Applications		Activity	TC [c] (cm^2/hr)	DFR [d] (µg/cm^2)	LADD [e] (mg/kg bw/day)	Cancer Risk [f]	REI [g] (days)
	Per year [a]	Rates [b] (kg a.i./ha)						
			hand weeding, propping, orchard maintenance	100	1.26	6.38E-05	6E-07	0.5
			transplanting	230	1.26	1.47E-04	1E-06	0.5
			scouting, hand pruning, training	580	1.26	3.70E-04	4E-06	0.5
			hand harvesting	1400	1.26	8.93E-04	9E-06	0.5
			thinning fruit	3000	0.53	8.97E-04	9E-06	0.5
			hand weeding, hand pruning	70	0.62	2.19E-05	2E-07	0.5
			scouting	210	0.62	6.57E-05	6E-07	0.5
			transplanting	230	0.62	7.19E-05	7E-07	0.5
			hand harvesting, tying/training	1100	0.62	3.44E-04	3E-06	0.5

Crop	Applications		Activity	TC [c] (cm^2/hr)	DFR [d] (µg/cm^2)	LADD [e] (mg/kg bw/day)	Cancer Risk [f]	REI [g] (days)
	Per year [a]	Rates [b] (kg a.i./ha)						
			irrigation (hand set)	1750	0.62	5.47E-04	5E-06	0.5
			hand weeding, thinning plants	70	0.88	3.11E-05	3E-07	0.5
			scouting	210	0.88	9.33E-05	9E-07	0.5
			scouting, hand harvesting	1100	0.88	4.89E-04	5E-06	0.5
			irrigation (hand set)	1750	0.88	7.77E-04	8E-06	0.5
			hand weeding, thinning plants	70	0.88	3.11E-05	3E-07	0.5
			scouting	210	0.88	9.33E-05	9E-07	0.5
			hand harvesting, roguing	1100	0.88	4.89E-04	5E-06	0.5
			scouting, thinning plants, hand harvesting	1300	0.88	5.77E-04	6E-06	0.5
			irrigation (hand set)	1750	0.88	7.77E-04	8E-06	0.5
			hand weeding	4400	0.41	9.16E-04	9E-06	0.5
			hand weeding	70	0.18	6.20E-06	6E-08	0.5
			transplanting	230	0.18	2.04E-05	2E-07	0.5
			scouting, hand harvesting	1100	0.18	9.74E-05	1E-06	0.5
			irrigation (hand set)	1750	0.18	1.55E-04	2E-06	0.5
			transplanting	230	0.81	9.41E-05	9E-07	0.5
			scouting, hand pruning, hand weeding, bird control, frost control, propagating, trellis repair	640	0.81	2.62E-04	3E-06	0.5
			hand harvesting	1400	0.81	5.73E-04	6E-06	0.5
			irrigation (hand set)	1750	0.81	7.16E-04	7E-06	0.5
			tying/training, hand harvesting, leaf pulling	8500	0.34	1.44E-03	1E-05	2
			girdling, turning	19300	0.15	1.46E-03	1E-05	15
			transplanting	230	0.88	1.02E-04	1E-06	0.5
			scouting, thinning plants, hand harvesting, mechanically-assisted harvesting	1300	0.88	5.77E-04	6E-06	0.5
			irrigation (hand set)	1750	0.88	7.77E-04	8E-06	0.5
			scouting, topping, tying/training	4000	0.41	8.33E-04	8E-06	0.5
			hand weeding	4400	0.41	9.16E-04	9E-06	0.5
			hand harvesting	5150	0.41	1.07E-03	1E-05	0.5
			hand weeding	70	1.16	4.11E-05	4E-07	0.5
			scouting, bird control	90	1.16	5.28E-05	5E-07	0.5

Crop	Applications		Activity	TC [c] (cm^2/hr)	DFR [d] (µg/cm^2)	LADD [e] (mg/kg bw/day)	Cancer Risk [f]	REI [g] (days)
	Per year [a]	Rates [b] (kg a.i./ha)						
			scouting	210	1.16	1.23E-04	1E-06	0.5
			scouting	1100	1.16	6.45E-04	6E-06	0.5
			irrigation (hand set)	1750	1.16	1.03E-03	1E-05	0.5
			hand detasseling, hand harvest	8800	0.33	1.48E-03	1E-05	8
Greenhouse cucumber, tomato	6	0.15	All activities	1400	2.25	1.59E-03	2E-05	0.5
			All activities	230	1.26	1.47E-04	1E-06	0.5
			Irrigation (hand set)	1750	1.26	1.12E-03	1E-05	0.5
			hand weeding, thinning plants	70	0.88	3.11E-05	3E-07	0.5
			scouting	210	0.88	9.33E-05	9E-07	0.5
			transplanting	230	0.88	1.02E-04	1E-06	0.5
			hand harvesting	1100	0.88	4.89E-04	5E-06	0.5
			hand harvesting, scouting, thinning plants	1300	0.88	5.77E-04	6E-06	0.5
			irrigation (hand set)	1750	0.88	7.77E-04	8E-06	0.5
			hand weeding	4400	0.41	9.16E-04	9E-06	0.5
			hand weeding, hand pruning	70	0.95	3.37E-05	3E-07	0.5
			scouting	210	0.95	1.01E-04	1E-06	0.5
			transplanting	230	0.95	1.11E-04	1E-06	0.5
			hand harvesting, tying/training	1100	0.95	5.29E-04	5E-06	0.5
			irrigation (hand set)	1750	0.95	8.42E-04	8E-06	0.5
			hand weeding, scouting	90	0.58	2.63E-05	3E-07	0.5
			transplanting	230	0.58	6.71E-05	7E-07	0.5
			hand harvesting, mechanically-assisted harvesting, canopy management	800	0.58	2.33E-04	2E-06	0.5
			irrigation (hand set)	1750	0.58	5.11E-04	5E-06	0.5
			hand weeding	100	0.18	8.85E-06	9E-08	0.5
			transplanting	230	0.18	2.04E-05	2E-07	0.5
			hand pruning, scouting	580	0.18	5.13E-05	5E-07	0.5
			seed cone harvest	1400	0.18	1.24E-04	1E-06	0.5
			irrigation (hand set)	1750	0.18	1.55E-04	2E-06	0.5
			seeding production harvest	6700	0.18	5.93E-04	6E-06	0.5

TC = transfer coefficient; DFR = dislodgeable foliar residue; LADD = Lifetime Average Daily Dose; REI = restricted entry interval

[a] The label listed maximum number of applications per year.

[b] The label listed maximum application rates.

[c] Transfer coefficients are from ARTF (2008).
[d] Based on dislodgeable foliar residue data on day 0 using the minimum interval between applications. Shaded cells indicate a TWA value over 30 days was used in the LADD calculation.
[e] Lifetime average daily dose = (Absorbed daily dose × activity days (30) × working duration (40 yrs))/ (365 days/year × life expectancy (78 yrs)); Absorbed Daily Dose = DFR × TC × 8 hr × DA/80 kg.; A dermal absorption value of 12% was included in the dermal component of the ADD
[f] A q_1^* value of 0.00987 (mg/kg bw/day)$^{-1}$ was considered appropriate to use in the cancer risk assessment. Cancer risks in the range of 1×10^{-5} were considered to be acceptable. Shaded cells indicate cancer risks greater than 1×10^{-5}; however, due to conservatisms in the risk assessment, these cancer risks were considered to be acceptable.
[g] Restricted entry interval = day at which cancer risks < 1×10^{-5}.

Table 7 Residential Applicator Exposure and Risk Assessment

Scenario	Formulation	Application Equipment	Application Type	Application Rate[a]	ATPD[b]	Dermal Exposure[c] (mg/kg bw/day)	Inhalation Exposure[e] (mg/kg bw/day)	Dermal MOE[d]	Inhalation MOE[f]
	Liquid	MPHW		0.00516 kg a.i./L	18.9 L	0.17	4.88E-05	2900	1300000
		Aerosol		7.88E-04 kg a.i./can	1 can	0.008	6.51E-05	62000	1000000
		Trigger sprayer		0.009675 kg a.i./bottle	1 bottle	0.023	1.57E-05	22000	4100000
	Liquid	MPHW		0.004195 kg a.i./L	18.9 L	0.14	3.97E-05	3600	1600000
		Aerosol can		0.000908 kg a.i./can	2 cans	0.019	1.50E-04	27000	430000
		Trigger sprayer		0.016125 kg a.i./bottle	2 bottles	0.076	5.24E-05	6600	1200000
Outdoor Fogging/Misting Systems	Ready-to-use	OASS	Space spray	0.0007875 kg a.i./day		0.008	6.51E-05	62000	1000000
		MPHW	Broadcast, perimeter		1.89 L	0.018	2.96E-04	27000	220000
		Paint brush	Perimeter		1 L	0.064	2.84E-05	7800	2300000
			Broadcast		1 can	0.020	1.64E-04	25000	400000
			Perimeter		0.5 can	0.010	8.21E-05	49000	790000
			Space spray	0.00516 kg a.i./can	0.25 can	0.013	1.07E-04	38000	610000
			Broadcast		1 bottle	0.042	2.93E-05	12000	2200000
			Perimeter		0.5 bottle	0.021	1.47E-05	24000	4400000
		Aerosol can	Pet	0.000635 kg a.i./pet		0.029	1.16E-04	17000	560000
			Pet	0.00375 kg a.i./pet		0.17	6.83E-04	3000	95000
			Pet	0.000398 kg a.i./horse	26 horses	0.23	9.42E-04	2100	69000
		Spot-on	Pet	0.0026 kg a.i./pet	2 pets	0.017	Negligible	29000	NA

MPHW = Manually pressurized handwand; OASS = Outdoor aerosol space spray; NA = Not applicable; ATPD = Area treated or amount handled per day
[a] Trigger sprayer and space spray application rates based on net contents, maximum guarantee, and density.

[b] Based on Residential SOP defaults (USEPA, 2012), Statistics Canada (2011), and professional judgement.
[c] Where dermal exposure (mg/kg bw/day) = (unit exposure × AR × ATPD)/80 kg. Dermal absorption is not required because the dermal NOAEL is based on a dermal toxicity study.
[d] MOE = margin of exposure; MOE = NOAEL/Exposure, based on a dermal NOAEL of 500 mg/kg bw/day and a target MOE of 300, applicable to short-, intermediate-, and long-term scenarios.
[e] Where inhalation exposure (mg/kg bw/day) = (unit exposure × AR × ATPD)/80 kg.
[f] MOE = NOAEL/Exposure, based on a inhalation NOAEL of 65 mg/kg bw/day and a target MOE of 300 applicable to short-, intermediate-, and long-term scenarios.

Table 8 Residential Applicator Cancer Risk Assessment

Scenario	Formulation	Application Equipment	Application Type	Treatment Frequency [a] (days/year)	LADD [b] (mg/kg bw/day)	Cancer Risk [c]
	Liquid	MPHW	Broadcast		9.03E-05	9E-07
		Aerosol	Spot		4.55E-06	4E-08
		Trigger sprayer	Broadcast		1.21E-05	1E-07
	Liquid	MPHW			7.34E-05	7E-07
		Aerosol			1.05E-05	1E-07
		Trigger sprayer			4.04E-05	4E-07
Outdoor Fogging/Misting Systems	Ready-to-use	OASS	Space spray	3	6.83E-06	7E-08
		MPHW	Broadcast, perimeter	12	6.70E-05	7E-07
		Paint brush	Perimeter		3.41E-05	3E-07
			Broadcast		1.15E-05	1E-07
			Perimeter		5.74E-06	6E-08
			Space spray		7.46E-06	7E-08
			Broadcast		2.26E-05	2E-07
			Perimeter		1.13E-05	1E-07
		Aerosol can	NA		2.63E-05	3E-07
			Pets		1.55E-04	2E-06
			Horses		2.14E-04	2E-06
		Spot-on [d]	NA		1.52E-05	2E-07

MPHW = Manually pressurized handwand; OASS = Outdoor aerosol space sprays; ADD = Absorbed daily dose; LADD = Lifetime average daily dose
[a] Treatment frequency is based maximum values provided on the label when available. When this information was not available ORETF survey data was used (Johnson et al., 1999).
[b] LADD = ADD × treatment frequency × exposure duration/(365 days × 78 years). Exposure duration = 63 years (35 years for pet treatments). ADD = (Dermal exposure × Dermal absorption (12%)) + Inhalation exposure. Exposure values from Table IV.7.
[c] A q_1^* value of 0.00987 $(mg/kg\ bw/day)^{-1}$ was considered appropriate to use in the cancer risk assessment. Cancer risks in the range of 1×10^{-6} were considered to be acceptable. Shaded cells indicate cancer risks that are more than 1×10^{-6}; however, due to conservatisms in the risk assessment, these cancer risks were considered to be acceptable.
[d] Dermal exposure only as inhalation is considered negligible for spot-on treatments (USEPA, 2012).

Table 9 Residential Postapplication Dermal Exposure and Risk Assessment

Exposure Scenario			Lifestage	TR [a] (µg/cm²)	TC [b] (cm²/hr)	ET [c] (hr/day)	Dermal Dose [d] (mg/kg bw/day)	MOE [e]
Short-, Intermediate-, Long-term Exposure								
			Adult		180000	1.5	0.589	850
			Youth		148000	1.3	0.589	850
			Children 1<2		49000	1.5	1.17	430
			Adult		5500	1	0.012	42000
			Youth		4500	1	0.014	36000
			Adult		5300	4	0.046	11000
			Youth		4400	4	0.054	9300
			Children 6<11		2900	4	0.063	7900
			Adult		8400	2.2	1.17	430
			Youth		6900	1.1	0.67	740
			Children 6<11		4600	1.1	0.80	620
			Adult		1700	1	0.11	4600
			Youth		1400	0.5	0.06	8000
			Children 6<11		930	0.5	0.07	6800
			Adult		220	1	8.46E-03	59000
			Youth		180	0.5	4.86E-03	100000
			Children 6<11		120	0.5	5.77E-03	87000
			Adult		180000	1.5	0.12	4300
			Youth		148000	1.3	0.12	4300
			Children 1<2		49000	1.5	0.23	2200
			Adult		180000	1.5	0.04	13000
			Youth		148000	1.3	0.04	13000
			Children 1<2		49000	1.5	0.08	6600
			Adult		6800	8	0.69	730
			Youth		5600	5	0.50	1000
			Children 1<2		1800	4	0.66	760
			Adult		6800	2	0.26	1900
			Youth		5600	1	0.15	3400
			Children 1<2		1800	2	0.49	1000
			Adult		6800	8	0.34	1500
			Youth		5600	5	0.25	2000
			Children 1<2		1800	4	0.33	1500
			Adult		6800	2	0.13	3900
			Youth		5600	1	0.074	6700
			Children 1<2		1800	2	0.25	2000

Exposure Scenario			Lifestage	TR [a] (µg/cm²)	TC [b] (cm²/hr)	ET [c] (hr/day)	Dermal Dose [d] (mg/kg bw/day)	MOE [e]
	Crack and Crevice	Carpet	Adult	0.10	6800	8	0.069	7300
			Youth		5600	5	0.05	10000
			Children 1<2		1800	4	0.066	7600
			Adult		6800	2	0.03	19000
			Youth		5600	1	0.01	34000
			Children 1<2		1800	2	0.05	10000
			Adult		6800	8	0.093	5400
			Youth		5600	5	0.067	7400
			Children 1<2		1800	4	0.090	5600
			Adult		6800	2	0.03	14000
			Youth		5600	1	0.02	25000
			Children 1<2		1800	2	0.067	7400
			Adult		6800	8	0.005	100000
			Youth		5600	5	0.003	140000
			Children 1<2		1800	4	0.005	110000
			Adult		6800	2	0.002	280000
			Youth		5600	1	0.001	480000
			Children 1<2		1800	2	0.003	140000
			Adult		5200	0.77	0.21	2400
			Youth		4300	0.92	0.29	1700
			Children 1<2		1400	1	0.54	930
			Adult		5200	0.77	0.18	2800
			Youth		4300	0.92	0.25	2000
			Children 1<2		1400	1	0.46	1100
			Adult		5200	0.77	0.34	1500
			Youth		4300	0.92	0.47	1100
			Children 1<2		1400	1	0.87	580
			Adult		5200	0.77	0.42	1200
			Youth		4300	0.92	0.59	850
			Children 1<2		1400	1	1.08	460

TR = Transferable residue; TC = Transfer coefficient; ET = Exposure time; MOE = Margin of exposure; OASS = Outdoor aerosol space spray; AR = application rate; Min = minimum; Max = maximum

[a] Transferable residue calculated based on the application rate and the exposure scenario using permethrin specific fraction transferred values of 1% for turf, 25% for gardens and trees, 2% for carpets, and 3% for hard surfaces (USEPA, 2012). For some scenarios (OASS) this value is the deposited residue based on calculations using the application rate. The minimum domestic application rate (1.23 kg a.i./ha) was assessed for lawns and turf as the maximum Canadian application rate (20.16 kg a.i./ha) showed risks of concern. The maximum Canadian rate in domestic gardens was assessed for gardens and trees (1.23 kg a.i./ha).

[b] Transfer coefficient default values from the Residential SOPs (2012) were used.

[c] Exposure time default values from the Residential SOPs (2012) were used.

[d] Dermal dose = TR × TC × ET/BW (kg) Body weights of 80, 57, 19, and 11 kg were used for adults, youths (11 <16 years), children (3 <6 years), and children (1 <2 years) respectively, as stated in the USEPA Residential SOPs (2012). Dermal absorption not required because the dermal NOAEL is based on a dermal toxicity study.

[e] MOE = NOAEL/ exposure, based on a dermal NOAEL of 500 mg/kg bw/day and a target MOE of 300 applicable to short-, intermediate-, long-term scenarios.

Table 10 Residential Postapplication Inhalation Exposure and Risk Assessment

Exposure Scenario			Lifestage	C_0 or Mass a.i. [a] (mg/m^3)	Exposure Time [b] (hr/day)	Inhalation Dose [c] (mg/kg bw/day)	MOE [d]
Short-, Intermediate-, Long-term Exposure							
			Adult		NA	1.2E-03	55000
			Youth		NA	1.6E-03	39000
			Children 1<2		NA	4.5E-03	15000
			Adult		1.5	2.7E-03	24000
			Youth		1.3	3.3E-03	20000
			Children 1<2		1.5	1.0E-02	6400
			Adult		2	0.021	3100
			Youth		2	0.029	2200
			Children 1<2		2	0.079	820
			Adult		2	13.2	5
			Youth		2	18.2	4
			Children 1<2		2	49.3	1
			Adult		16	3.1E-05	2100000
			Youth		15	4.0E-05	1600000
			Children 1<2		18	1.3E-04	490000

OASS = Outdoor aerosol space spray; Co = Initial concentration; MOE = Margin of exposure

[a] OASS application rate in mg a.i./day used. Indoor space spray initial concentration calculated based on the application rate. Indoor surface spray mass of a.i. calculated based on the amount of a.i. applied.

[b] Exposure time based on default values from the Residential SOPs (2012).

[c] Inhalation dose calculated based on calculations from the Residential SOPs (2012) .

[d] MOE = NOAEL/ exposure, based on a dermal NOAEL of 65 mg/kg bw/day and a target MOE of 300 applicable to short-, intermediate-, long-term scenarios.

Table 11 Residential Postapplication Incidental Oral Exposure and Risk Assessment for Children (1< 2 years old)

Exposure Scenario			Hand/Object/Soil Residue [a] (mg/cm^2)	ET [b] (hr/day)	Oral Dose [c] (mg/kg bw/day)	MOE [d]
Short-term Exposure						
		HtM	9.63E-04		0.009	2600
		OtM	1.23E-04		0.00051	45000
		Soil ingestion	8.24 µg/g	NA	3.7E-05	610000
Outdoor Fogging/Misting System	OASS (3 apps, 14 day interval)	HtM	8.2E-05	1.5	7.9E04	29000
		Carpet	2.3E-04	4	6.2E-03	3700
		Hard surface	3.4E-04	2	4.6E-03	4900
		Carpet	1.1E-04	4	3.1E-03	7400

Exposure Scenario			Hand/Object/Soil Residue [a] (mg/cm²)	ET [b] (hr/day)	Oral Dose [c] (mg/kg bw/day)	MOE [d]
		Hard surface	1.7E-04	2	2.3E-03	9900
		Carpet	2.3E-05	4	6.2E-04	37000
		Hard surface	3.4E-05	2	4.6E-04	49000
		Carpet	3.1E-05	4	8.4E-04	27000
		Hard surface	4.6E-05	2	6.3E-04	36000
		Carpet	1.6E-06	4	4.3E-05	530000
		Hard surface	2.4E-06	2	3.3E-05	710000
		Carpet	1.0	4	1.3E-02	1700
		Hard surface	1.5	2	9.9E-03	2300
		Carpet	0.50	4	6.6E-03	3500
		Hard surface	0.76	2	4.9E-03	4600
		Carpet	0.10	4	1.3E-03	17000
		Hard surface	0.15	2	9.9E-04	23000
		Carpet	0.14	4	1.8E-03	13000
		Hard surface	0.21	2	1.3E-03	17000
		Carpet	0.007	4	9.2E-05	250000
		Hard surface	0.011	2	6.9E-05	330000
		Small	2.0E-04	1	0.0013	3700
		Medium	1.7E-04	1	0.0011	4400
		Large	3.2E-04	1	0.0022	2300
	HtM Cat	All	4.0E-04	1	0.0027	1900
Long-term Exposure						
		Carpet	1.6E-04	4	3.8E-03	1300
		Hard surface	2.4E-04	2	2.9E-03	1700
		Carpet	8.1E-05	4	1.9E-03	2600
		Hard surface	1.2E-04	2	1.4E-03	3500
		Carpet	1.6E-05	4	3.8E-04	130000
		Hard surface	2.4E-05	2	2.8E-04	170000
		Carpet	2.2E-05	4	5.2E-04	9500
		Hard surface	3.3E-05	2	3.9E-04	13000
		Carpet	1.2E-06	4	2.7E-05	190000
		Hard surface	1.7E-06	2	2.0E-05	250000
		Carpet	1.0	4	1.2E-02	400
		Hard surface	1.5	2	9.4E-03	530
		Carpet	0.50	4	6.2E-03	800
		Hard surface	0.75	2	4.7E-03	1100
		Carpet	0.10	4	1.2E-03	4000
		Hard surface	0.15	2	9.4E-04	5300

Exposure Scenario			Hand/Object/Soil Residue [a] (mg/cm²)	ET [b] (hr/day)	Oral Dose [c] (mg/kg bw/day)	MOE [d]
	OtM Fogger	Carpet	0.14	4	1.7E-03	2900
		Hard surface	0.21	2	1.3E-03	3900
		Carpet	0.007	4	8.8E-05	57000
		Hard surface	0.011	2	6.6E-05	76000

OASS = Outdoor aerosol space spray; ET = Exposure time; MOE = Margin of exposure; HtM = Hand-to-Mouth; OtM = Object-to-Mouth; Apps = applications; AR = application rate

[a] Based on the dermal postapplication exposure from indoor applications without the body weight × fraction of a.i. on hands compared to the body (0.15)/(4 hr × 4 intervals/hr).

[b] Exposure time based on default values from the Residential SOPs (2012).

[c] Oral dose = [Hand Residue (mg/cm²) × (Fraction of hand mouthed/event (0.13) × Surface Area of one hand (150 cm²)) × (Exposure Time (hr) × Replenishment Intervals (4/hr)) × (1 − (1 − Saliva Extraction Factor (0.48)) $^{\text{Number events per hour (20)/Replenishment Intervals (4/hr)}}$)]/ Body Weight (11 kg).

[d] MOE = Point of departure/Exposure, based on an oral $BMDL_{20}$ of22.95 mg/kg bw/day and a target MOE of 300 applicable to short-term exposure.

Table 12 Residential Postapplication Dermal Cancer Risk Assessment

Exposure Scenario			Lifestage	TWA TR [a] (µg/cm²)	Refined TC [b] (cm²/hr)	ADD [c] (mg/kg bw/day)	LADD [d] (mg/kg bw/day)	Lifetime Cancer Risk [f]
			Adult		NA	3.25E-02	2.15E-03	
			Youth		NA	3.25E-02	1.71E-04	
			Children 1<2		NA	6.43E-02	3.39E-04	
			Adult		NA	6.61E-04	4.39E-05	
			Youth		NA	7.59E-04	4.00E-06	
			Adult		NA	2.55E-03	1.69E-04	
			Youth		NA	2.97E-03	1.56E-05	
			Children 6<11		NA	3.49E-03	1.84E-05	
			Adult		3200	1.56E-02	1.04E-03	
			Youth		2600	8.91E-03	4.69E-05	
			Children 6<11		1800	1.10E-02	5.79E-05	
			Adult		NA	2.96E-03	1.97E-04	
			Youth		NA	1.71E-03	9.03E-06	
			Children 6<11		NA	2.03E-03	1.07E-05	
			Adult		200	2.12E-04	1.40E-05	
			Youth		160	1.19E-04	6.26E-07	
			Children 6<11		110	1.45E-04	7.66E-07	
			Adult		NA	6.5E-03	4.3E-04	
			Youth		NA	6.5E-03	3.4E-05	
			Children 1<2		NA	1.3E-02	6.7E-05	
			Adult		4700	5.64E-02	3.74E-03	
			Youth		3900	4.11E-02	2.16E-04	
			Children 1<2		1300	5.67E-02	2.99E-04	
			Adult		4700	2.12E-02	1.40E-03	

Exposure Scenario			Lifestage	TWA TR [a] (µg/cm²)	Refined TC [b] (cm²/hr)	ADD [c] (mg/kg bw/day)	LADD [d] (mg/kg bw/day)	Lifetime Cancer Risk [f]
			Youth		3900	1.23E-02	6.49E-05	
			Children 1<2		1300	4.25E-02	2.24E-04	
			Adult		4700	2.82E-02	1.87E-03	
			Youth		3900	2.05E-02	1.08E-04	
			Children 1<2		1300	2.84E-02	1.49E-04	
			Adult		4700	1.06E-02	7.02E-04	
			Youth		3900	6.16E-03	3.24E-05	
			Children 1<2		1300	2.13E-02	1.12E-04	
			Adult		4700	5.64E-03	3.74E-04	
			Youth		3900	4.11E-03	2.16E-05	
			Children 1<2		1300	5.67E-03	2.99E-05	
			Adult		4700	2.12E-03	1.40E-04	
			Youth		3900	1.23E-03	6.49E-06	
			Children 1<2		1300	4.25E-03	2.24E-05	
			Adult		4700	7.74E-03	5.14E-04	
			Youth		3900	5.63E-03	2.97E-05	
			Children 1<2		1300	7.78E-03	4.10E-05	
			Adult		4700	2.90E-03	1.93E-04	
			Youth		3900	1.69E-03	8.90E-06	
			Children 1<2		1300	5.84E-03	3.07E-05	
			Adult		4700	3.98E-04	2.64E-05	
			Youth		3900	2.90E-04	1.53E-06	
			Children 1<2		1300	4.00E-04	2.11E-06	
			Adult		4700	1.49E-04	9.90E-06	
			Youth		3900	8.69E-05	4.58E-07	
			Children 1<2		1300	3.00E-04	1.58E-06	
			Adult	1.92 mg/day	3600	2.88E-03	1.06E-04	
			Youth	1.35 mg/day	3000	2.83E-03	1.49E-05	
			Children 1<2	1.04 mg/day	980	1.14E-02	6.00E-05	
			Adult	1.63 mg/day	3600	2.45E-03	9.04E-05	
			Youth	1.14 mg/day	3000	2.41E-03	1.27E-05	
			Children 1<2	0.89 mg/day	980	9.69E-03	5.10E-05	
			Adult	3.09 mg/day	3600	4.64E-03	1.71E-04	
			Youth	2.17 mg/day	3000	4.56E-03	2.40E-05	
			Children 1<2	1.68 mg/day	980	1.84E-02	9.67E-05	
			Adult	3.84 mg/day	3600	5.76E-03	2.13E-04	
			Youth	2.69 mg/day	3000	5.66E-03	2.98E-05	
			Children 1<2	2.09 mg/day	980	2.28E-02	1.20E-04	

TWA = Time weighted average; TR = Transferable residue; TC = Transfer coefficient; ET = Exposure time; ADD = Absorbed Daily Dose; LADD = Lifetime average daily dose; OASS = Outdoor aerosol space spray; NA = Not applicable; apps = Applications; AR = application rate

[a] TWA transferable residue calculated based on the application rate and the exposure scenario and time weighted over 30 days using a daily dissipation rate of 6% for outdoor applications and 13% for pet applications. The minimum domestic application rate (1.23 kg a.i./ha) was assessed for lawns and turf as the maximum Canadian application rate (20.16 kg a.i./ha) showed risks of concern. The maximum Canadian rate was assessed domestic gardens and trees (1.23 kg a.i./ha). For indoor scenarios, dissipation data is not available; therefore, a TWA TR could not be calculated and the TR from the non-cancer risk assessment was used for the cancer risk assessment. For treated pets a TWA exposure per day was calculated using the equation provided in the Res SOPs (2012).

[b] Transfer coefficient values refined to the 50th percentile from the Residential SOPs (2012) were used when available.

[c] ADD = TR × TC × ET × Dermal absorption (12%) /BW (kg) Body weights of 80, 57, 19, and 11 kg were used for adults, youths (11 <16 years), children (3 <6 years), and children (1 <2 years) respectively, as stated in the USEPA Residential SOPs (2012). 50th percentile values for exposure time were used for the gardens and trees and treated pet scenarios. 50th percentile values for fraction transferred were used for the indoor environment scenario.

[d] LADD = ADD × exposure frequency × exposure duration/(365 days × 78 years). Exposure frequency = 30 days/year. Exposure duration = 63 years (35 years for pet treatments and 16 years for military).

[e] A q_1^* value of 0.00987 (mg/kg bw/day)$^{-1}$ was considered appropriate to use in the cancer risk assessment. Cancer risks in the range of 1×10^{-6} were considered to be acceptable for residential exposure. Shaded cells indicate cancer risks greater than 1×10^{-6}.

[f] Lifetime cancer risk = sum of cancer risk over all 3 lifestages.

Table 13 Residential Postapplication Inhalation Cancer Risk Assessment

Exposure Scenario			Lifestage	TWA C_o or Mass a.i. [a] (mg/m^3)	ADD [b] (mg/kg bw/day)	LADD [c] (mg/kg bw/day)	Lifetime Cancer Risk [d]
			Adult	NA	1.19E-03	7.92E-05	
			Youth	NA	1.65E-03	8.68E-06	
			Children 1<2	NA	4.47E-03	2.36E-05	
			Adult		2.72E-03	1.81E-04	
			Youth		2.32E-03	1.22E-05	
			Children 1<2		1.40E-03	7.39E-06	
			Adult		5.59E-03	3.71E-04	
			Youth		7.72E-03	4.07E-05	
			Children 1<2		2.10E-02	1.10E-04	
			Adult		2.67	1.77E-01	
			Youth		3.69	1.94E-02	
			Children 1<2		10.00	5.27E-02	
			Adult	NA	3.08E-05	2.05E-06	
			Youth	NA	3.95E-05	2.08E-07	
			Children 1<2	NA	1.32E-04	6.98E-07	

OASS = Outdoor aerosol space spray; Co = Initial concentration; LADD = Lifetime average daily dose; NA = not applicable; TWA = Time weighted average; ADD = Absorbed Daily Dose

[a] TWA values could not be calculated for OASS, mosquito abatement and surface spray air concentrations; therefore, air concentrations used for the non-cancer risk assessment were used for the cancer risk assessment. Indoor space spray values were time weighted over 2 hours for indoor space spray applications.

[b] ADD = Exposure (mg/day) /BW (kg) Body weights of 80, 57, 19, and 11 kg were used for adults, youths (11 <16 years), children (3 <6 years), and children (1 <2 years) respectively, as stated in the USEPA Residential SOPs (2012).

[c] LADD = ADD × exposure frequency × exposure duration/(365 days × 78 years). Exposure frequency = 30 days/year. Exposure duration = 63 years. ADD = Inhalation dose calculated based on calculations from the Residential SOPs; exposure time based on default values from the Residential SOPs (2012).

[d] A q_1^* value of 0.00987 (mg/kg bw/day)$^{-1}$ was considered appropriate to use in the cancer risk assessment. Cancer risks in the range of 1×10^{-6} were considered to be acceptable. Shaded cells indicate cancer risks greater than 1×10^{-6}. Lifetime cancer risk = sum of cancer risk over all 3 lifestages.

[e] The maximum calculated application rate was used to determine cancer risk for space spray application because this application rate was based on label instructions and represents a more typical application rate.

Table 14 Residential Postapplication Incidental Oral Cancer Risk Assessment for Children

Exposure Scenario			LADD [a] (mg/kg bw/day)	Cancer Risk [b]
		HtM	2.2E-05	2E-07
		OtM	2.7E-06	3E-08
		Soil ingestion	2.0E-06	2E-09
Outdoor Fogging/Misting System	OASS (3 apps, 14 day interval)	HtM	4.2E-06	4E-08
		Carpet	2.0E-05	2E-07
		Hard surface	1.5E-05	1E-07
		Carpet	1.0E-05	1E-07
		Hard surface	7.6E-06	7E-08
		Carpet	2.0E-06	2E-08
		Hard surface	1.5E-06	1E-08
		Carpet	2.8E-06	3E-08
		Hard surface	2.1E-06	2E-08
		Carpet	1.4E-07	1E-09
		Hard surface	1.1E-07	1E-09
		Carpet	6.6E-05	7E-07
		Hard surface	4.9E-05	5E-07
		Carpet	3.3E-05	3E-07
		Hard surface	2.5E-05	2E-07
		Carpet	6.6E-06	7E-08
		Hard surface	4.9E-06	5E-08
		Carpet	9.0E-06	9E-08
		Hard surface	6.8E-06	7E-08
		Carpet	4.6E-07	5E-09
		Hard surface	3.5E-07	3E-09
		Small	7.2E-06	7E-08
		Medium	6.1E-06	6E-08
		Large	1.2E-05	1E-07
	Cat	All	1.4E-05	1E-07

OASS = Outdoor aerosol space spray; ET = Exposure time; LADD = Lifetime average daily dose; ADD = Absorbed daily dose; apps = Applications; AR = Application rate; HtM = Hand-to-mouth; OtM = Object-to-mouth.

[a] LADD = ADD × exposure frequency × exposure duration (365 days × 78 years). Exposure frequency = 30 days/year. Exposure duration = 5 years. ADD = Oral dose = [Hand Residue (mg/cm^2) × (Fraction of hand mouthed/event (0.13) × Surface Area of one hand (150 cm^2)) × (Exposure Time (hr) ÷ Replenishment Intervals (4 hr)) × (1 − (1 − Saliva Extraction Factor (0.48))$^{\text{Number events per hour (2)/Replenishment Intervals (4 hr)}}$)] / Body Weight (11 kg). Hand residue is based on the dermal postapplication exposure from indoor applications without the body weight × fraction of a.i. on hands compared to the body (0.15) (4 hr ÷ 4 intervals/hr). 50th percentile values for fractions of hand mouthed, number of hand-to-mouth events were used when refinement was necessary. Hand residue was weighted over 30 days for hand-to-mouth exposure on treated lawns; exposure time based on default values from the Residential SOPs (2012).

[b] A q_1^* value of 0.00987 (mg/kg bw/day)$^{-1}$ was considered appropriate to use in the cancer risk assessment. Cancer risks in the range of 1 × 10^{-6} were considered to be acceptable.

Table 15 Summary of Co-occurring Exposures; Short-, Intermediate-term Exposure

Scenario	Lifestage	Co-occurring Exposures [a]
	Adult	Applicator inhalation exposure Dietary exposure
	Children 1<2	Hand-to-mouth exposure Dietary exposure
Gardens & Trees [b,c]	Adult	Applicator inhalation exposure Dietary exposure
	Adult	Applicator inhalation exposure Postapplication inhalation exposure Dietary exposure
	Youth	Postapplication inhalation exposure Dietary exposure
	Children 1<2	Postapplication inhalation exposure Hand-to-mouth exposure Dietary exposure
	Adult	Postapplication inhalation exposure Dietary exposure
	Youth	Postapplication inhalation exposure Dietary exposure
	Children 1<2	Postapplication inhalation exposure Hand-to-mouth exposure Dietary exposure
	Adult	Applicator inhalation exposure Postapplication inhalation exposure Dietary exposure
	Youth	Postapplication inhalation exposure Dietary exposure
	Children 1<2	Postapplication inhalation exposure Hand-to-mouth exposure Dietary exposure
	Adult	Postapplication dermal exposure Postapplication inhalation exposure Dietary exposure
	Youth	Postapplication dermal exposure Postapplication inhalation exposure Dietary exposure
	Children 1<2	Postapplication dermal Postapplication inhalation exposure Hand-to-mouth exposure Dietary exposure
	Adult	Applicator inhalation exposure Dietary exposure
	Children 1<2	Hand-to-mouth exposure Dietary exposure
Military Clothing	Adult	Applicator dermal exposure Postapplication dermal exposure

[a] Only exposure that had toxicological significance to the aggregate assessment are listed. For short-, intermediate-term exposure there is no dermal aggregate endpoint. All scenarios were considered to be short-, intermediate-term exposure except for indoor environments, which also considered long-term exposure.
[b] No postapplication inhalation exposure is expected.
[c] Only children aged 6<11 years are expected to conduct activities in gardens; therefore, no incidental oral exposure is expected.
[d] Applicator exposure was not considered to be long-term exposure.

Table 16 Aggregate Non-Cancer Exposure Risk Assessment

Scenario	Lifestage	Dermal Exposure [a] (mg/kg bw/day	Dermal MOE [b]	Inhalation Exposure [c] (mg/kg bw/day)	Inhalation MOE [b]	HtM Exposure [d] (mg/kg bw/day)	Chronic Dietary Exposure [e] (mg/kg bw/day)	Total Oral Exposure [f] (mg/kg bw/day)	Oral MOE [b]	Aggregate MOE [g]
	Adult	NA	NA	6.51E-05	1000000	NA	0.000146	0.000146	34000	33000
	Children	NA	NA	NA	NA	8.98E-03	0.000271	0.00925	540	540
Gardens & Trees	Adult	NA	NA	1.50E-04	430000	NA	0.000146	0.000146	34000	32000
	Adult	NA	NA	1.26E-03	52000	NA	0.000146	0.000146	34000	21000
	Youth	NA	NA	1.65E-03	39000	NA	0.000113	0.000113	44000	21000
	Children	NA	NA	4.47E-03	15000	4.97E-04	0.000271	0.000768	6500	4500
	Adult	NA	NA	2.72E-03	24000	NA	0.000146	0.000146	3400	14000
	Youth	NA	NA	3.26E-03	20000	NA	0.000113	0.000113	4400	14000
	Children	NA	NA	1.02E-02	6400	8.98E-03	0.000271	0.00925	540	500
	Adult	NA	NA	2.11E-02	3800	NA	0.000146	0.000146	34000	2800
	Youth	NA	NA	2.92E-02	2200	NA	0.000113	0.000113	44000	2100
	Children	NA	NA	7.91E-02	820	6.19E-03	0.000271	0.00646	770	400
	Adult	0.69	729	3.10E-05	730	NA	0.000146	0.000146	3400	710
	Youth	0.50	1010	4.00E-05	1000	NA	0.000113	0.000113	4400	990
	Children	0.66	758	1.30E-04	760	6.19E-03	0.000271	0.00646	774	380
	Adult	NA	NA	9.40E-04	69000	NA	0.000146	0.000146	34000	23000
	Children	NA	NA	NA	NA	2.70E-03	0.000271	0.00297	1700	1700

NA = not applicable; HtM = Hand-to-mouth;

[a] There is no short-, intermediate-term dermal aggregate endpoint, as such; aggregate dermal exposure is only applicable to long-term scenarios. As applicator exposure is considered to be short-, intermediate-term, it was not included in the long-term aggregate assessment.

[b] MOE = NOAEL or NOAEC (mg/kg bw/day)/Exposure (mg/kg bw/day). Short-, intermediate-term aggregate endpoints for oral, and inhalation exposure are 5 mg/kg bw/day and 65 mg/kg bw/day, respectively. Long-term aggregate endpoints for oral, dermal, and inhalation exposure are 5 mg/kg bw/day, 500 mg/kg w/day, and 65 mg/kg bw/day, respectively. Target MOE is 300.

[c] Inhalation exposure from applicator exposure was included in the adult inhalation exposure value, when applicable.

[d] Hand-to-mouth exposure is only applicable to children 1 – 2 years old.

[e] Chronic dietary exposure is based on information provided in the dietary risk assessment.

[f] Total Oral Exposure = HtM exposure + Chronic dietary exposure

[g] Aggregate MOE = 1/((1/MOE dermal) + (1/MOE inhalation) + (1/MOE oral))

Table 17 Aggregate Non-Cancer Exposure and Risk Assessment for Permethrin using Biomonitoring Data

Sub-population	Metabolite(s)	Specific Metabolite Daily Excretion [a] (µg/kg bw/day)	Fue [b]	Parent Equivalent [c] (µg/kg bw/day)	Aggregate MOE [d] Target = 300
CHMS/MIREC					
General Population (6-79 years)		0.113		0.54	9200
Children (<3 years)[e]		0.146		0.70	7100
Children (3-5 years)[f]		0.275		1.32	3800
Children (6-10 years)		0.0512		0.25	20,000
Youth (11-15 years)		0.149		0.72	7000
Adult (16-79 years)		0.121		0.58	8600
Literature Studies [h]		**Urinary Metabolite Concentration (µg/L)**			
Lu, et al. 2009 (3-11 years)		9.6		2.63	1900
Wu, et al., 2013 (1 year)		17.4		4.75	1050
Naeher, et al. 2010 (4-6 years)		19.9		5.44	920

N/A = not applicable; CHMS = Canadian Health Measures Survey; MIREC = Maternal-Infant Research on Environmental Chemicals; Fue = Urinary Extraction Fraction; MOE = Margin of Exposure

[a] These are the urinary metabolite concentrations (µg/g creatinine) normalized by each individual's body weight (kg) and excreted creatinine (determined for each individual based on their age, height and weight). CHMS data was used for adults, youth and children older than 3. MIREC-CD plus data was used for children under 3 years old. The 95th percentile values were used in the risk assessment, except for where the CV was greater than 33% in the CHMS data. For these values, the upper 95% confidence bound of the 95th percentile was used in the risk assessment, as is recommended by Statistics Canada for the CHMS data.

[b] Urinary excretion fraction. Based on human pharmacokinetic study (Ratelle,*et al.*, 2015) and is the sum of the excreted fractions (molar % of total dose) for cis (10.3%) and trans-DCCA (25.9%).

[c] Calculated using the following equation: Specific metabolite daily excretion (µg/kg bw/day) ÷ ($MW_{parent}/MW_{metabolite}$)/ Fue (%).

[d] Aggregate MOE = NOAEL/parent equivalent. MOEs are calculated using the permethrin short-, intermediate-term aggregate NOAEL.

[e] Data from MIREC-CD plus

[f] Cycle 2 data only

[g] Exposure was calculated using the 'cis- + trans-DCCA' urinary concentration summed for each individual for CHMS and MIREC-CD plus

[h] 95th percentiles values from the literature studies, where reported. See Table 3.15 for more information.

[i] As cis and trans-DCCA metabolites were reported separately, metabolite concentrations were summed. It is unknown if these high values would be excreted by the same individual and is an uncertainty in the risk assessment; however, it is not expected to underestimate exposure.

Table 18 Aggregate Cancer Exposure and Risk Assessment for Permethrin

Sub-Population	Exposure Duration	LADD [a] (µg/kg bw/day)	Lifetime Cancer Risk [b]
General population (6-79 years)	74 years	0.211	
Children (<6 years)	5 years	0.00264	

[a] LADD (lifestage average daily dose) was calculated for the general population and children < 6 years old using the following equation: LADD = urinary metabolite concentration from CHMS × (MW parent/MW metabolite) × exposure duration (74 years for the general population, 5 years for children) × daily excretion (g creatinine/day) /(urinary excretion fraction from human pharmacokinetic studies × body weight × lifetime (79 years) × 1000 µg/mg).

[b] Lifetime Cancer risks for the general population were calculated using the following equation: Lifetime Cancer Risk = $LADD_{Gen\ pop} + LADD_{Children\ (<6\ yrs)} \times q_1^*$. $q_1^* = 9.87 \times 10^{-1}$ (mg/kg bw/day)$^{-1}$

Appendix III Dietary Exposure and Risk Estimates for Permethrin

Table 1 Summary of Acute Dietary Exposure and Risk from Permethrin

Population Subgroup	Food only – 95th Percentile		Food and Drinking Water – 95th Percentile	
	Exposure (mg/kg bw)	%ARfD[1]	Exposure (mg/kg bw)	%ARfD[1]
General Population	0.008610	10.76	0.008787	11
All Infants (< 1 year old)	0.008157	10.20	0.008644	11
Children 1- 2 years old	0.012424	15.53	0.012472	16
Children 3 - 5 years old	0.011749	14.69	0.011929	15
Children 6 - 12 years old	0.008322	10.40	0.008433	11
Youth 1 - 19 years old	0.006917	8.65	0.007070	9
Adults 20 - 49 years old	0.008665	10.83	0.008886	11
Adults 50+ years old	0.008273	10.34	0.008418	11
Females 13 -49 years old	0.009214	11.52	0.009375	12

[1] Acute Reference Dose (ARfD): 0.08 mg/kg bw

Table 2 Summary of Chronic Dietary Exposure and Risk from Permethrin

Population Subgroup	Non-cancer			
	Food only		Food and drinking water	
	Exposure (mg/kg bw)	%ADI[1]	Exposure (mg/kg bw)	%ADI[1]
General Population	0.000112	0.6	0.000149	1
All Infants (< 1 year old)	0.000185	0.9	0.000323	2
Children 1 - 2 years old	0.000228	1.1	0.000279	1
Children 3 - 5 years old	0.000207	1.0	0.000248	1
Children 6 - 12 years old	0.000131	0.7	0.000162	1
Youth 13 - 19 years old	0.000089	0.4	0.000115	1
Adults 20 - 49 years old	0.000106	0.5	0.000143	1
Adults 50+ years old	0.000095	0.5	0.000131	1
Females 13 - 49 years old	0.000098	0.5	0.000134	1

[1] Acceptable daily intake (ADI): 0.02 mg/kg bw/day

Table 3 Summary of Cancer Dietary Exposure and Risk from Permethrin

Population Subgroup	Food Only		Food and Drinking Water	
	Exposure (mg/kg bw/day)	Cancer Risk[1]	Exposure (mg/kg bw/day)	Cancer Risk[1]
General Population	0.000112	1E-06	0.000149	1E-06

[1] Potency factor (q_1^*): 9.87×10^{-3} $(mg/kg\ bw/day)^{-1}$

Calculated risk based on mitigation with the number of applications in tomatoes reduced.

Appendix IV Food Residue Chemistry Summary

The *Food and Drugs Act* prohibits the sale of food containing a pesticide residue that exceeds the specified maximum residue limit (MRL). Pesticide MRLs are specified for *Food and Drugs Act* purposes through the evaluation of scientific data under the *Pest Control Products Act*. Each MRL value defines the maximum concentration parts per million (ppm) of a pesticide allowed in or on certain foods when a pesticide is used according to label directions, and serves as a food safety standard. The Canadian Food Inspection Agency is responsible for monitoring the Canadian food supply for pesticide residues and the determination of compliance with MRLs specified by Health Canada. MRLs are established in Canada for residues of permethrin on domestic commodities and certain imported crops. Residues in all other agricultural commodities are regulated under Subsection B.15.002(1) of the *Food and Drugs Regulations*, which requires that residues do not exceed 0.1 parts per millions (ppm). A complete list of MRLs specified in Canada can be found in the Pest Management Regulatory Agency's (PMRA) MRL Database, an online query application that allows users to search for MRLs, regulated under the *Pest Control Products Act*, for both pesticides and food commodities http://pr-rp.hc-sc.gc.ca/mrl-lrm/index-eng.php).

The nature of the permethrin residue in livestock and plant commodities is adequately understood based on metabolism studies in cabbage, sweet corn, soybean, goats (oral), cows (oral and dermal) and hens (oral and dermal). The metabolism of permethrin is similar in plants and animals. It occurs by cleavage of the ester linkage of permethrin to form 3-(2,2-dichloroethenyl)-2,2-dimethylcyclopropane-1-carboxylic acid (DCVA) and (3-phenoxyphenyl)methanol (MPBA). Further oxidation of these metabolites results in the formation of diacid and lactone form of DCVA, 3-phenoxybenzoic acid (3-PBA), 4-hydroxy-phenoxybezoic acid (4-OH-3-PBA), and/or 4-hydroxy-(3-phenoxyphenyl)methanol (4-OH-MPBA). Permethrin was found consistently as the major residue in all tested matrices, except kidney and liver of ruminants, and liver of poultry. Metabolites DCVA, MPBA and/or 3-PBA were identified as significant residues in certain plant and animal commodities.

The residue definition in plant and animal commodities is currently expressed as the parent compound, (3-phenoxyphenyl)methyl 3-(2,2-dichloroethenyl)-2,2-dimethylcyclopropanecarboxylate, for both risk assessment and enforcement purposes. Several field trial data, animal feeding studies and environmental fate studies have become available to the PMRA after the establishment of this residue definition. This new information indicates the occurrence of significant amounts of DCVA, MPBA and/or 3-PBA in certain plant and animal commodities as well as in drinking water. The toxicological effects of these metabolites cannot be excluded. Therefore, for risk assessment purposes, the residue definition in plant and animal commodities was revised as "sum of isomers of permethrin for commodities where permethrin is the only major residue; and sum of isomers of permethrin, isomers of DCVA, MPBA and/or 3-PBA for commodities where permethrin and its metabolites are major residues." For drinking water risk assessment, the residue definition of "sum of isomers of permethrin, isomers of DCVA, MPBA and 3-PBA" was established. For enforcement purposes, the residue definition in plant and animal matrices is proposed to remain the same as the current definition, (3-phenoxyphenyl)methyl 3-(2,2-dichloroethenyl)-2,2-dimethylcyclopropanecarboxylate, considering that the parent chemical is a suitable marker for residues of permethrin.

Analytical methods were developed for data generation in plant and animal matrices using gas chromatography (GC) coupled with electron capture detection (ECD) or mass spectrometry (MS), high performance liquid chromatography (HPLC) coupled with ultraviolet-visible spectrophotometry (UV-Vis), and thin-layer chromatography (TLC). For enforcement of permethrin *per se* in animal and plant matrices, adequate GC-ECD methods are available. In addition, permethrin is included in the scope of multi-residue analytical methods (MRMs) used by the US Food and Drug Administration and the Canadian Food Inspection Agency's National Chemical Residue Monitoring Program. These enforcement methods and MRMs have been validated by independent laboratories, and therefore fulfill the requirements for enforcement purposes.

Residue chemistry data for confined crop rotational studies and field accumulation in rotational crops are acceptable. Based on the available data, a plant back interval of 60 days for non-registered crops is required on all agricultural product labels of permethrin.

Available residue data support the established MRLs for permethrin and, therefore, are deemed adequate.

Use directions, including maximum application rates and pre-slaughter interval (PSI), are not specified on some product labels for sheep and horse. Since the available residue data on cattle support a PSI of 1 day, it is proposed to include a PSI of 1 day on all labels for sheep and horse (including revision of labels that have a PSI of 90 days). In addition, some use directions are not specified on labels of a number of permethrin products registered for use on livestock animals and animal housing; therefore, it is proposed to update the labels to reflect the use conditions from the submitted animal studies and from registrant feedback. The label updates would include application rates, maximum number of applications, minimum re-treatment interval and/or PSI in the product labels, where applicable. See Appendix IX for specific label statements.

Data Gaps

No residue chemistry data are required as a result of permethrin re-evaluation. However, the following data gaps were identified:

- DACO 7.3 Storage stability data on permethrin and/or its metabolites in animal commodities; and
- DACO 7.4 Food and/or feed crop residue trial study, including food/feed handling establishments, for certain crops.

These data gaps may need to be addressed for future use expansions.

Appendix V Fate, Toxicity, and Risks to the Environment

Table 1a Summary of Fate Processes for Permethrin in the Terrestrial and Aquatic Environment - Abiotic and Biotic Transformation

Process	$T_{1/2}$ or DT_{50} (days)	DT_{90}	Kinetics (T_R or $T_{1/2slow}$)	Comments	PMRA Reference (original study / foreign review)
Abiotic transformation					
Hydrolysis 25°C	pH 5: Stable pH 7: Stable pH 9: 60 d (*cis* isomer) 40 d (trans isomer)	NR	SFO	Not a major route of transformation	1131731 / 2431484
Hydrolysis 25°C	pH 3, 6 and 9: Stable	NR	SFO	In the USEPA 2006 EFED review, permethrin is listed as relatively stable at pH 9 ($T_{1/2}$ = 125 – 350 days).	1137720 / 2431484
Phototransformation soil (25°C, 30 days)	106	NR	SFO	Not a major route of transformation	2431484
Phototransformation soil (25°C, 4.53 %OC)	254 - 324	NR	SFO		
Phototransformation soil	104	NR	SFO		
Aquatic Phototransformation pH 5, 25°C	51 - 71	nr	SFO	Not a major route of transformation.	2431490
Aquatic Phototransformation pH 5, 25°C	85	nr	SFO	Sunlight equivalent to 30°N latitude (1998 EU Draft report)	European Union 1998 EU; PMRA 2431487
Aquatic phototransformation (seawater)	14	nr	SFO	May be an important route of transformation in seawater.	2431490
Aerobic Soil Biotransformation					
Freshsham sandy loam: 365d, 0.36 lbs a.i./acre	37	NR	NR	Slightly persistent. Cited as supplemental in 2006 USEPA EFED.	2431484
Freshsham sandy loam: 32d	7 - 113	NR	SFO	The study investigated the effect of different application solvent volumes, type of solvent, soil moisture and method of application on mineralization and half-lives.	2431491
Sandy loam: 25°C, 32d, ^{14}C-cyclopropyl label 1 and 13 mg a.i./kg soil, ^{14}C-cyclopropyl labeled permethrin	1mg/kg soil: 19 - 23 13 mg/kg soil: 86 - 113	NR	NR	Slightly persistent	2431484
5 soils: 16 weeks (20°C for 15 hours and 9 hours at 10°C daily) 1 mg a.i./kg permethrin (60:40 cis:trans)	Soil half-lives were reported as ≤ 3 weeks for 4 soils and > 14 weeks for 1 soil. Raw data was not available; based on visual inspection of Figure 1 and 2 of study, the half-lives reported for soils with $T_{1/2}$ ≤ 3 weeks appear to be accurate.			Slightly to moderately persistent	2431484
	Dubbs fine sandy loam: ^{14}C-*cis* and *trans*-carbonyl label (224 g				

Process	$T_{1/2}$ or DT_{50} (days)	DT_{90}	Kinetics (T_R or $T_{1/2slow}$)	Comments	PMRA Reference (original study / foreign review)
	a.i./ha)				
25°C, 128d, ^{14}C-*cis* and ^{14}C-*trans* carbonyl labeled permethrin (224 and 2242 g a.i./ha)	*Cis:* 19.9 *Trans:* 10.8 Combined: 15.2	*Cis:* 66 *Trans:* 35.9 Combined: 50.6	SFO		
	Dubbs fine sandy loam: ^{14}C-*cis* and *trans*-carbonyl label (2242 g a.i./ha)				
	Cis: 24 *Trans:* 11.9 Combined: 17.3	*Cis:* 79.8 *Trans:* 39.4 Combined: 57.3	SFO		
	Memphis silt loam: ^{14}C-*cis* and *trans*-carbonyl label (224g a.i./ha)				
	Cis: 42.6 *Trans:* 11.7 Combined: 24.4	*Cis:* 142 *Trans:* 39 Combined: 81.2	SFO		
	Memphis silt loam: ^{14}C-*cis* and *trans*-carbonyl label (2242g a.i./ha)				
	Cis: 41.1 *Trans:* 11.2 Combined: 24.3	*Cis:* 137 *Trans:* 37.3 Combined: 80.9	SFO		
5 soils: 28d, 25°C. ^{14}C-carbonyl and ^{14}C-methylene labeled permethrin (224 g a.i./ha)	Soil half-lives were reported as < 28 days. The results are consistent with those of other aerobic soil studies, however, soils were analyzed only at test termination (day 28).			Slightly persistent	1131674
Two Japanese soils: 25°C. ^{14}C dichlorovinyl and ^{14}C methylene labeled permethrin (1 mg a.i./kg)	*Trans:* 6 – 9 *Cis:* 12	NR	NR	Non-persistent	WHO 1990; PMRA 2677257
	^{14}C cyclopropyl *cis-trans* label (2242 g a.i./ha)				
	Cis: 14.2 *Trans:* 5.21 Combined: 7.96	*Cis:* 114 *Trans:* 17.3 Combined: 26.4	34.3 (IORE) SFO SFO		
	^{14}C-methylene-*cis* label at 224 g a.i./ha)				
	Cis: 1.88	*Cis:* 18.3	5.5 (IORE)		
	^{14}C-methylene-*cis* label at 2224 g a.i./ha)				
	Cis: 6.48	*Cis:* 37.6	11.3 (IORE)		
	10°C				
	Cis: 45.9 *Trans:* 16.9 Combined: 37.6	*Cis:* 153 *Trans:* 56.3 Combined: 125	SFO		
	25°C				
	Cis: 13.7 *Trans:* 5.39 Combined: 10.4	*Cis:* 356 *Trans:* 17.9 Combined: 226	107 (IORE) SFO 68 (IORE)		
	40°C				
	Cis: 34.3 *Trans:* 2.9 Combined: 16	*Cis:* 114 *Trans:* 23.5 Combined: 135	SFO 8.6 (DFOP) 52.4 (DFOP)		

Process	$T_{1/2}$ or DT_{50} (days)	DT_{90}	Kinetics (T_R or $T_{1/2slow}$)	Comments	PMRA Reference (original study / foreign review)
Mineral and organic soil 16 weeks	The half-life in mineral and organic soil is reported as approximately 2 and 3 weeks, respectively. Based on visual inspection of Figure 1 of study, the half-lives reported appear to be accurate.			Slightly persistent	1248501
4 soils 15, 25 and 35°C, 14 weeks ^{14}C-*cis* permethrin, ^{14}-*trans*-permethrin, ^{14}C *cis-trans* permethrin (60:40)	Half-lives were not calculated in the study; the study authors report that more than 50% of permethrin was transformed after 1.5 weeks incubation in soil and more than 90% after 9 week.			Slightly persistent	1131679
2 soils; R-*cis* and S-*cis* permethrin Arlington soil: pH 6.7, 0.82 %OM, 20°C San Diego Creek sediment: pH 7.9, 1.09% OM, 20°C	R-*Cis*: 124 S-*Cis*: 102 R-*Cis*: 124 S-*Cis*: 126	NR	SFO	Moderately persistent	2431482
Anaerobic Soil Biotransformation					
	^{14}C- *trans*-carbonyl label				
	224 g a.i./ha: 61 2242 g a.i./ha : 50	202 167	SFO		
Sandy loam soil: pH 6.6, 3.3% OM. 24°C, 30 days aerobic followed by 60 days flooded anerobic. ^{14}C-cyclopropyl and ^{14}Cphenyl *cis-trans* permethrin (ratio not reported); 13 mg a.i./kg.	^{14}C-cyclopropyl label: 180 ^{14}C-phenyl label: 226	598 751	SFO	Persistent	1131672
Soil, 25°C No other details reported.	197	NR	NR	Persistent	2431490
2 soils; R-*cis* and S-*cis* permethrin Arlington soil: pH 6.7, 0.82 %OM, 20°C San Diego Creek sediment: pH 7.9, 1.09% OM, 20°C	R-*Cis*: 114 S-*Cis*: 102 R-*Cis*: 99 S-*Cis*: 122	NR	SFO	Moderately persistent	2431482
Aerobic aquatic biotransformation					
Water : sediment system	38 - 43	NR	NR	Slightly persistent	2431484
Anaerobic aquatic biotransformation					
Water : sediment system	113 - 175	NR	NR	Slightly persistent	2431484

DFOP = double first order in parallel; IORE = Indeterminate Order Rate Equation model; nr = not reported; OC = organic carbon content; OM = organic matter content; SFO = single first order
NR = Not Reported

Table 1b Summary of Fate Processes for Permethrin in the Terrestrial and Aquatic Environment – Mobility

Process	Soil type	K_d or K_f (1/n)	K_{oc}	Comments	PMRA Reference (original study / foreign review)
	ERTC sandy loam	Kf = 1420	Kfoc = 491000		
	Chamberlains loamy sand	Kf = 2420	Kfoc = 139000		
	Hyde Farm sandy loam	Kf = 2100	Kfoc = 190000		
	Frensham sandy loam	Kf = 1970	Kfoc = 170000		
	Sand	Kf = 140	Kfoc = 194000		
	Sandy loam	Kf = 217	Kfoc = 34100		
	Clay loam	Kf = 246	Kfoc = 31500		
	Silt loam	Kf = 236	Kfoc = 28200		
	Sediment sandy loam	Kf = 401	Kfoc = 96600		
	Sand	Kf = not determined	Kfoc = not determined	Very highly mobile	
	Silty clay	Kf = 3.11	Kfoc = 122	Highly mobile	
	Sandy loam	Kf = 0.98	Kfoc = 118	Highly mobile	
	Sandy loam	Kf = 2.44	Kfoc = 215	Medium mobility	
	Sand	Kf = not determined	Kfoc = not determined	Very highly mobile	
	Silty clay	Kf = 0.46	Kfoc = 18	Very highly mobile	
	Sandy loam	Kf = 0.16	Kfoc = 19	Very highly mobile	
	Sandy loam	Kf = 0.54	Kfoc = 48	Very highly mobile	
Soil column leaching (soil aged 30 days)	74 – 78% of the ^{13}C activity remained in the upper 0 - 1 inch layer of the columns; all material in the leachate was *trans*-DCVA (13.7% of AR).				2431484
Soil column leaching (2 soils: incubated 0 and 21 days)	When a mixture with no pre-incubation was applied to the column, only 1.0 to 3.4% of AR was found in lower layer and no radiocarbon was eluted. When 14C-permethrin preincubated with soil for 21 days was applied on top of a soil column and eluted with water, 7.9-17.2% of the applied radiocarbon was recovered in the lower layers of the column and 0.3 - 2.6% was found in leachate.Permethrin was not detected in the leachate.				WHO 1990; PMRA 2677257

* K_f - Freundlich adsorption coefficient; K_{foc} - Coefficient adsorption per organic carbon ($K_f \times 100$/% organic carbon)

Table 1c Summary of Fate Processes for Permethrin in the Terrestrial and Aquatic Environment – Field Studies

Process	$T_{1/2}$ or DT_{50} (days)	DT_{90}	Kinetics (T_R or $T_{1/2slow}$)	Comments	PMRA Reference (original study / foreign review)
Terrestrial field studies					
Halifax County, North Carolina Silty loam: 1.0% OM	6	20	SFO	Non-persistent	1131690 / 2431484
Champaign County, Illinois	1	34			

Process	$T_{1/2}$ or DT_{50} (days)	DT_{90}	Kinetics (T_R or $T_{1/2slow}$)	Comments	PMRA Reference (original study / foreign review)
Silty clay loam: 3.0% OM					
Marion, Arkansas (soil characteristics not reported)	DT_{50}/DT_{90} values could not be calculated due to an inadequate number of sampling events in which permethrin was shown to decrease in soil. There was no apparent difference between the rates of dissipation between the *cis* and trans isomers. Based on visual inspection of the data the DT_{50} of permethrin would be >30 days and <90 days.				1131684
Marion, Arkansas Sandy loam: 1.0 % OM	*Cis:* 27.4 *Trans:* 11.2 Combined: 15.3	90.9 37.1 50.8	SFO		
Davis, California Sandy loam: 1.74 % OM	*Cis:* 57.8 *Trans:* 43.1 Combined: 43.7	192 143 145	SFO		
Greenwood, Nebraska Silt loam: 3.6% OM	*Cis:* 19.1 *Trans:* 10.1 Combined: 12.7	63.4 33.5 42.2	SFO		
Gasport, New York Silt loam: 2.3% OM	*Cis:* 58.9 *Trans:* 32.4 Combined: 38.3	196 108 127	SFO		
Soil (characteristics, location not reported)	6 - 106	NR	NR	Range reported in the WFD-UKTAG review of permethrin. No other details were provided.	2431486
Illinois, California, three west German field sites (soil characteristics not reported)	6 - 28	52 - 92	SFO	Range reported in the EU Draft Report and Proposed Decision Document for permethrin. No other details were provided.	2431489
Aquatic field studies					
Outdoor mesocosm: California pond (10 applications at 78.4 g a.i./ha at one day intervals)	*Cis-* and *trans*-permethrin dissipated from pond water with a calculated half-life of 1.8 and 1.4 days, respectively (the main removal mechanism is adsorption to suspended solids and sediment in the water column, not degradation. In sediment the reported half-life of *cis* and *trans*-permethrin was 118 and 18 days, respectively. *Cis-* and *trans*-permethrin appeared to be immobile and remained in the upper 0–2 inch sediment fraction.				
Outdoor mesocosm: North Carolina pond (10 applications at 78.4 g a.i./ha at one day intervals)	*Cis-/trans*-permethrin dissipated from pond water with a registrant calculated half-life of 3.1 and 1.9 days, respectively. In sediment the reported half-life of cis/*trans*-permethrin was 256 and 62 days, respectively. *Cis*-permethrin and *trans*-permethrin appeared to be immobile and remained in the upper 0–2 inch sediment fraction.				
Lotic systems: Forest streams in the boreal forest region of the Gaspe Peninsula, Quebec, near Geraldton in Northern Ontario, and in the Acadian forest region near Fredericton, New Brunswick.	Aerial spraying (17.5 g a.i./ha): nine applications - three single swaths applied to a stream channel, and the remaining six were applications to forest blocks through which a stream flowed. All applications included direct overspray of the streams. The mean calculated half- life of permethrin in stream water from 17 oversprayed sites was determined to be 10.3 hours (range = 1.8-20.4 hours). Sites located downstream of application had a mean calculated half- life of 3.9 hours (range = 2.3 – 6.4 hours). Partitioning of permethrin from stream water to sediments at concentrations above the limit of detection (5 ng/g) was infrequent and sporadic.				Kreutzweiser 1991 (PMRA 2431495) WHO 1990 (PMRA 2677257)
Outdoor mesocosm: Two pond experiments (1 application at 28 g a.i./ha -^{14}C cyclopropyl or methylene position, 60:40 *Cis:*trans)	In the first experiment (1979), permethrin levels in water decreased from 15.5 µg/L at 2 hours postapplication to 3.3 µg/L at 12 hours postapplication, and were below the LOD (0.01 µg/L) after 7 days. In the second experiment (1980), permethrin levels in water decreased from 29.0 µg/L at 2 hours-post application to 2.2 µg/L at 48 hours post application and reached the LOD by day 35. Sediment was shown to be the major sink for permethrin in the ponds.				Rawn *et al.* 1982 (PMRA 2665075)
Lotic system: cold-water forest stream in the Lake Superior	Permethrin reached a peak concentration of 11.8 µg/L five minutes after treatment 30 m downstream of the treatment site and decreased to below detection after 240 minutes. At 730 m downstream, permethrin reached a peak concentration of 0.1µg/L after 360 minutes				2431492

Process	$T_{1/2}$ or DT_{50} (days)	DT_{90}	Kinetics (T_R or $T_{1/2slow}$)	Comments	PMRA Reference (original study / foreign review)
watershed (Ambush EC 500 g a.i./L)	which decreased to 0.02 µg/L at 480 minutes. Results demonstrated that aquatic invertebrates, plants and stream detritus act as major sinks for permethrin; the study duration was not sufficient to determine the persistence of residues within these substrates. Permethrin was no longer detected in fish after 360 minutes which would indicate that the clearance time is fish is relatively fast.				
Outdoor mesocosms: Permethrin (Permasect 230 g/L EC) was applied at 8 g a.i./ha and 80 g a.i./ha to the surface of two individual mesocosms.	The mass balance for permethrin at day 1 was 26.3 – 30% Residual concentrations of permethrin in the tank receiving the 8 g a.i./ha could not be measured in the water phase. Permethrin was not detected in the sediment phase in tanks that received 8 or 80 g a.i./ha. In water, permethrin dissipated rapidly with none detectable by day 14. Volatilization during spraying and immediately after from the water surface is suggested as the reason for the rapid initial loss of permethrin from the test systems.				Bromilow *et al.*, 2006 (PMRA 2664987)
Lotic system: Permethrin (1.3 g each of the *cis*- and *trans*-isomers) were added to a New Zealand upland stream.	The mass losses and concentration changes over a 545 m downstream reach were quantified over a three hour period following application. Peak concentrations of permethrin declined exponentially with elapsed time SFO half-lives of 116 and 75 minutes were estimated for *cis* and *trans*-permethrin, respectively.				Wilcock R.J., *et al.*, 1994 (PMRA 2665084)

NR = Not Reported; OM = organic matter content; SFO = single first order

Table 2 Summary of toxicity of permethrin to non-target terrestrial species.

Effects on terrestrial organisms					
Organism	**Exposure**	**Test substance**	**Endpoint value**	**Comment / Toxicity classification[a]**	**Reference**
Invertebrates					
Earthworm (*Lumbricus* and *Allolobophora spp.*)		Not Reported	Non-statistically significant decrease in populations at 12.3 kg a.i./ha, no effect at 1.23 kg a.i./ha.	NA	USEPA. 2008
Earthworm (*Eisenia fetida*)		Sanathrin 250 EC 247.27 g/L	14 day LC_{50}: 22.1 mg a.i./kg dry weight NOEC: <15.63 mg a.i./kg dw (based on body weight)	NA	European Union 1998; PMRA 2431487
Earthworm (*Lampito mauritii*)		Not Reported	LC50 = > 1200 mg/kg dry weight soil	NA	WHO 2011; PMRA 2677259
Lumbricus terrestris and	Field Study	EC formulation (250 g a.i./L	No effects observed at 0.25 and 0.50 kg a.i./ha	NA	European Union 1998; PMRA 2431487

Effects on terrestrial organisms					
Organism	**Exposure**	**Test substance**	**Endpoint value**	**Comment / Toxicity classification[a]**	**Reference**
Allolobophora chlorotica			40-49% decline in numbers and 56-57% reduction in weight at 2.5-5.0 kg a.i./Ha		
Soil micro-organisms	Field Study	10% EC	Lower Sand Soil: Ammonification not affected at 0.7 and 14.0 mg as/kg soil Nitrification inhibited at 0.7 mg a.i./kg soil, but stimulated at 14 mg a.i./kg soil Carbon mineralization not affected	NA	European Union 1998; PMRA 2431487
Soil micro-organisms	Field Study	Sanathrin 250 EC 247.27 g/L	Carbon mineralization not affected over 28 days Nitrogen mineralization not affected	NA	European Union 1998; PMRA 2431487
Soil Microflora	Not reported	technical	No effect on the soil nitrogen turnover and short-term respiration in a field soil tested up to 6.875 kg of Permethrin technical/ha (corresponding to 5-fold application rate) 42 days after application.	NA	WHO 2011; PMRA 2677259
Soil Bacteria and fungi	Not reported	Ambush 5G 2.24 kg/ha	Permethrin suppressed bacterial and actinomycete populations in samples taken 1, 9, and 27 days after application, but control levels were re-gained after 41 days	NA	WHO 1990; PMRA 2677257
		Technical	48-h LD_{50} = 0.05 µg a.i./bee		
		Not reported	48-h LD_{50} = 0.16 µg a.i./bee		
		93.1%	48-h LD_{50} = 0.024 µg a.i./bee		
		25% formulation	48-h LD_{50} = 1.36 µg a.i./bee		European Union 1998; PMRA 2431487

Effects on terrestrial organisms					
Organism	**Exposure**	**Test substance**	**Endpoint value**	**Comment / Toxicity classification[a]**	**Reference**
	Acute Oral	Technical	48-h LD_{50} = 0.19 µg a.i./bee	Highly toxic	USEPA 2008; PMRA 2684727
		93.1%	48-h LD_{50} = 0.13 µg a.i./bee		
		25% formulation	48-h LD_{50} = 0.54 µg a.i./bee		European Union 1998; PMRA 2431487
	Foliar Residue	25WP	48-h LD_{50} <224 g a.i./Ha		
	Field Study - Canola	Ambush 25% EC	application of permethrin at rates up to 70 g as/Ha prior to bees actively foraging in canola had no significant effect on mortality, foraging ability or brood health. May have been a slight repllent effect for 5 days post-treatment		European Union 1998; PMRA 2431487
	Field Study - Apples	Ambush 25% EC	permethrin applied at 52 g as/Ha did not significantly affect bee mortality or performance. May be some evidence of a repellent effect on foraging activity immediately following application, but subsequent foraging activity was not affected.		European Union 1998; PMRA 2431487
	Field Study – corn	Ambush and Pounce	At the rates tested (37 g a.i./Ha × permethrin had no significant effect on bee mortality following application over the 3 year study. Was a high repellancy effect after application	NA	European Union 1998; PMRA 2431487
Stingless bees (*Melipona beecheii, Nannotrigona perilampoides and*	24-h contact	Technical	24-h LD_{50}s: 0.010 to 0.098 µg a.i./bee	NA	Valdovinos-Núñez *et al.* 2009 – PMRA 2665325

Effects on terrestrial organisms					
Organism	**Exposure**	**Test substance**	**Endpoint value**	**Comment / Toxicity classification[a]**	**Reference**
Trigona nigra)					
Andrena erythronii, *Megachile rotundata*, and *Bombus terricola*	48-h contact	Technical	48-h LD_{50}: *Andrena erythronii:* 0.008 µg a.i./bee *M. rotundata*: 0.018 µg a.i./bee *B. terricola:* 0.215 µg a.i./bee		Helson *et al.* 1994 – PMRA 2665324
Parasitic wasp (*Apanteles* sp.)	Acute, 5-d contact	3.2 EC	100% mortality at 0.2 lb a.i./A (224.2 g a.i./ha) 17% mortality at 0.1 lb a.i./A (112.1 g a.i./ha)		
Parasitic wasp (*Opius bruneipus*)	Acute, 5-d contact	3.2 EC	43% mortality at 0.2 lb a.i./A (224.2 g a.i./ha) 0% mortality at 0.1 lb a.i./A (112.1 g a.i./ha)		
Parasitic wasp (*Telenomus remus*)	Acute, 5-d contact	3.2 EC	90% mortality at 0.2 lb a.i./A (224.2 g a.i./ha) 13% mortality at 0.1 lb a.i./A (112.1 g a.i./ha)		
Parasitic wasp (*Copidosoma truncatellum*)	Acute, 2-d contact	3.2 EC	100% mortality at 0.2 lb a.i./A (224.2 g a.i./ha) 85% mortality at 0.1 lb a.i./A (112.1 g a.i./ha)		
Parasitic wasp (*Diglyphus intermedius*)	Acute, 5-d contact	3.2 EC	40% mortality at 0.2 lb a.i./A (224.2 g a.i./ha) 55% mortality at 0.1 lb a.i./A (112.1 g a.i./ha)		
Mite (*Amblyseium fallacis*)	Acute	25 EC	100% mortality at 0.5 ppm		
Mite (*Amblyseium*	Acute	Ambush	LC50 <1 ppm		

Effects on terrestrial organisms					
Organism	**Exposure**	**Test substance**	**Endpoint value**	**Comment / Toxicity classification[a]**	**Reference**
fallacis)					
Mite (*Amblyseium fallacis*)	Acute dip test	Formulated	LC50 <0.5 ppm		
Convergent ladybeetle (*Hippodamia convergens*)	Contact	Formulated	LD50<3.9 ppm		
Convergent ladybeetle (*Hippodamia convergens*)	Treated foliage	Fomulated	LD50=15.5 ppm		
Alfalfa leafcutter bee (*Megachile rotundata pacifica*)	Caged with treated foliage	Not reported	48-hour LD50 = 0.16 µg a.i./bee 24% to 88% mortality at rates of 0.5 oz. a.i./A and 2 o.z. a.i./A, respectively (35 and 140 g a.i./ha)		
Predatory mite (*Metaseiulus occidentalis*)	Acute	Ambush	LD50 <2.0 ppm		
Predatory mite (*Metaseiulus occidentalis*)	Acute, contact	25 EC	LD90 = 1–5 ppm		
Predatory mite (*Metaseiulus occidentalis*)	Acute, dip test	Formulated	LD50 <1 ppm		
Alkali bee (*Nomia melanderi*)	Caged with treated foliage	Not reported	48-h LD50 = 0.16 µg a.i./bee 25% to 78% mortality at rates of 0.5 oz. a.i./A and 2 o.z. a.i./A,		

Effects on terrestrial organisms					
Organism	**Exposure**	**Test substance**	**Endpoint value**	**Comment / Toxicity classification[a]**	**Reference**
			respectively (35 to 140 g a.i./ha)		
Seven spot ladybird (*Coccinella septempunctata*) and Eleven spot ladybird (*C. undecimpunctata*)	Field application to oil seed canola	Not reported	Significant reduction in numbers at rates of 15 ppm and higher, 24 h post-treatment.		
Hover flies (Syrphidae)	Field, spray application	Not reported	All rates of 31.2 ppm and above caused a reduction in the numbers of larvae and no larvae observed at 125 ppm.		
Six-spotted thrips (Scolothrips sexmaculatus)	Field,	25% a.i.	No significant reduction in numbers at 8 days post-treatment at 224.2 g a.i./ha (3.2 oz a.i./A).		
Hemipteran predators (*Geocoris pallens*) (*Orius tristicolor*) (*Nabis americoferris*)	Field	25% a.i.	Significant reduction in numbers at all rates tested 56, 112.1 and 224.2 g a.i./ha (0.8, 1.6 and 3.2 oz/A); populations temporarily eliminated.		
Unnamed spiders, mites and collembola	Spray application	Not reported	No effect at 0.5 kg a.i./A.		
	Laboratory	Treatment rate (g a.i./ha)	IOBC rating		European Union 1998; PMRA 2431487
Pterostichus melanarius (Adult)	Acute Contact Toxicity	90	Harmless		
Chrysopa carnea	Acute	30	Harmful		

Effects on terrestrial organisms					
Organism	**Exposure**	**Test substance**	**Endpoint value**	**Comment / Toxicity classification[a]**	**Reference**
(Larvae)	Contact Toxicity				
Venturia canescens (Adult)	Acute Contact Toxicity	75	Harmful		
Trichogramma cacoeciae (Adult)	Acute Contact	30	Harmful		
T. cacoeciae (Parasitised egg)	Acute Contact Activity	?	Moderately Harmful		
Amblyseius fallacis (Adult)	Acute Contact Toxicity	?	Harmful		
Carabidae *Pterostichus melanarius* *Harpalus spp.* *Agonum dorsale* Total carabidae			Significant reduction in abundance in week following spraying. No significant effect No significant effect All treated plots below control levels up to August.		
Staphylinidae *Philonthus cognatus* *Tachyporus Hypnorum* *Aleocharinae* Total Staphylinidae			Initial low levels in counts. No sign. effect increase in T. nitidulus. No significant effect All treated plots higher than controls.		

Effects on terrestrial organisms					
Organism	**Exposure**	**Test substance**	**Endpoint value**	**Comment / Toxicity classification[a]**	**Reference**
Araneae *Erigone atra* *Linyphiidae* *Lycosidae* *Total Araneae* *Hymenoptera* *Thysanoptera* *Collembola* *Coleoptera*			Significant reduction in abundance for 4 weeks post spraying. Lower than controls (N.S) Significant reduction in abundance for 4 weeks post spraying. Lower than control following spraying (N.S) Significant reduction No significant effect No significant effect		
Birds					
		95.7	LD_{50} (mg a.i./kg bw) >4,640 (24-h)		
		94.4	LD_{50} (mg a.i./kg bw) >2,000 (14-d)		
		Technical	LD_{50} (mg a.i./kg bw) >9,869 (male) (21 days) LD_{50} (mg a.i./kg bw) >10,327 (female)	Practically non-toxic	
Bobwhite quail (*Colinus virginianus*)		250 EC	LD_{50} = 2000 LD_{50} (mg a.i./kg bw) (15 days) NOEL = 125 LOEL = 250	Practically non-toxic	European Union 1998; PMRA 2431487
		Technical	LD_{50} (mg a.i./kg bw) >13,534 (24-h)	Practically non-toxic	USEPA (2008)
		Technical	LD_{50} (mg a.i./kg bw) >13,740 (male) (21-days) >15,345 (female)	Practically non-toxic	USEPA (2008)

Effects on terrestrial organisms					
Organism	**Exposure**	**Test substance**	**Endpoint value**	**Comment / Toxicity classification[a]**	**Reference**
Japanese quail [1] (*Coturnix coturnix*)		Technical	LD_{50} (mg a.i./kg bw) >20,000 (male) (24-h) >15,517 (female)	Practically non-toxic	USEPA (2008)
Starling [1] (*Sturnus vulgaris*)		Technical	LD_{50} (mg a.i./kg bw) >42,706 (24-h)	Practically non-toxic	USEPA (2008)
		95.7	LD_{50} (mg a.i./kg bw) >10,000	Practically non-toxic	
		93.4	LD_{50} (mg a.i./kg bw) >5,200	Practically non-toxic	
		92	LD_{50} (mg a.i./kg bw) >23,000	Practically non-toxic	
Northern bobwhite quail (*Colinus virginianus*)		93.4	LD_{50} (mg a.i./kg bw) >5,200	Practically non-toxic	
Northern bobwhite quail (*Colinus virginianus*)		95.7	LD_{50} (mg a.i./kg bw) >10,000	Practically non-toxic	
Japanese quail [1] (*Coturnix japonica*)		92	LD_{50} (mg a.i./kg bw) >23,000	Practically non-toxic	
Ring-necked pheasant (*Phasianus colchicus*)		92	LD_{50} (mg a.i./kg bw) >23,000	Practically non-toxic	
Mallard duck (*Anas Platyrhynchus*)		92.4	NOAEC/ LOAEC (mg a.i./kg-diet) 25/ >25 No Effect	No effect	
Mallard duck (*Anas Platyrhynchus*)		95.2	NOAEC/ LOAEC (mg a.i./kg-diet)125/500	Overall decrease in egg production	

Effects on terrestrial organisms					
Organism	**Exposure**	**Test substance**	**Endpoint value**	**Comment / Toxicity classification[a]**	**Reference**
Northern bobwhite quail (*Colinus virginianus*)		92.4	NOAEC/ LOAEC (mg a.i./kg-diet) 25/>25 No Effect	No effect	
Northern bobwhite quail (*Colinus virginianus*)		95.2	NOAEC/ LOAEC (mg a.i./kg-diet)500/ >500 No Effect	No effect	
Mammals					
Rat	Acute oral	39:61 *Cis*:trans 95.6%	LD50 = 806/814 mg/kg bw (/)		PMRA 1237289
Rat	Acute Inhalation	39:61 *Cis*:trans 85.6%	4-h LC_{50} = 2.30 g/L		PMRA 1237261
Rat	3-Generation Dietary Repro.	40:60 *Cis*:trans Purity not available	Parental and reproductive NOAELs = 67 mg/kg bw/day Offspring NOAEL = 33 mg/kg bw/day		PMRA #: 2127237, 2127238, 2127243, 2327215, 2327223
Vascular plants					
Monocot - (Wild oat (*Avena fatu*, Green Foxtail *Setaria viridis* Dicots – Lettuce *Lactuca sativa*, Tomato *Lycopersicon esculentum*	Pre and post emergence applications at 1.0 and 8.0 kg as/Ha		No effects		European Union 1998; PMRA 2431487
(*Allium cepa*, *Avena sativa*, *Beta vulgaris*,	Terrestrial plant tests – seedling emergence & seedling growth tests		Endpoints in mg/kg oven dried soil *Allium cepa* = LOER 1000, NOER 200		

Effects on terrestrial organisms					
Organism	**Exposure**	**Test substance**	**Endpoint value**	**Comment / Toxicity classification[a]**	**Reference**
Cucumia sativus, Glycine max, Helianthus annus)	93.07%		*Avena sativa* = LOER 8, NOER 1.6 *Beta vulgaris* = LOER 200, NOER 40 *Cucumia sativus* = LOER >1000, NOER 1000 *Glycine max* = LOER >1000, NOER 1000 *Helianthus annus* = LOER 40, NOER 8		
Allium cepa, Avena sativa, Beta vulgaris, Cucumia sativus, Glycine max Heiianthus annus	Terrestrial plant vegetative vigour test 93.07%		The most sensitive species for a reduction in biomass was *Allium cepa* at an application rate of 6875 g test item/ha. However, no effects were > 20%. WHO classified permethrin as low risk.		

Table 3 Screening level risk assessment for permethrin for birds and mammals at the highest single application rate for agricultural uses (pears – 425 g a.i./ha).

	Toxicity (mg a.i./kg bw/d)	Feeding Guild (food item)	EDE (mg a.i./kg bw)	RQ	LOC Exceeded?
Small Bird (0.02 kg)					
Acute	200[1]	Insectivore	34.59	0.17	No
Reproduction	7.07[2]	Insectivore	34.59	**4.89**	Yes
Medium Sized Bird (0.1 kg)					
Acute	200	Insectivore	27.00	0.13	No
Reproduction	7.07	Insectivore	27.00	**3.82**	Yes
Large Sized Bird (1 kg)					
Acute	200	Herbivore (short grass)	17.44	0.09	No
Reproduction	7.07	Herbivore (short grass)	17.44	**2.47**	Yes
Small Mammals (0.015 kg)					

	Toxicity (mg a.i./kg bw/d)	Feeding Guild (food item)	EDE (mg a.i./kg bw)	RQ	LOC Exceeded?
Acute	80.6	Insectivore	19.90	0.25	No
Reproduction	67.0	Insectivore	19.90	0.30	No
Medium Sized Mammals (0.035 kg)					
Acute	80.6	Herbivore (short grass)	38.59	0.48	No
Reproduction	67.0	Herbivore (short grass)	38.59	0.58	No
Large Sized Mammals (1 kg)					
Acute	80.6	Herbivore (short grass)	20.62	0.26	No
Reproduction	67.0	Herbivore (short grass)	20.62	0.31	No

[1] Based on the LD50 of 2000 mg a.i./kg diet foor mallard duck with a 10x uncertainty factor
[2] based on the NOEC of 125 mg a.i./kg diet converted to a daily dose using default feeding and bird weight parameters

Table 4a Refined avian risk assessment using maximum and mean permethrin residue values based on the highest crop application rate (pears - 425 g a.i./ha, respectively).

			Maximum nomogram residues				Mean nomogram residues			
			On-field		Off Field		On-field		Off Field	
	Toxicity (mg a.i./kg bw/d)	Food Guild (food item)	EDE (mg a.i./kg bw)	RQ	EDE (mg a.i./kg bw)	RQ	EDE (mg a.i./kg bw)	RQ	EDE (mg a.i./kg bw)	RQ
Small Bird (0.02 kg)										
Reproduction	7.07[1]	Insectivore	34.59	**4.9**	25.60	**3.6**	23.89	**3.38**	17.68	**2.50**
	7.07	Frugivore (fruit)	10.71	**1.5**	7.92	**1.1**	5.11	0.72	3.78	0.53
Medium Sized Bird (0.1 kg)										
Reproduction	7.07	Insectivore	27.00	**3.8**	19.98	**2.8**	18.64	**2.64**	13.79	**1.95**
	7.07	Frugivore (fruit)	8.36	**1.2**	6.18	0.9	3.99	0.56	2.95	0.42
Large Sized Bird (1 kg)										
Reproduction	7.07	Insectivore	7.88	**1.1**	5.83	0.8	5.44	0.77	4.03	0.57
	7.07	Herbivore (short grass)	17.44	**2.5**	12.90	**1.8**	6.19	0.88	4.58	0.65
	7.07	Herbivore (long grass)	10.65	**1.5**	7.88	**1.1**	3.48	0.49	2.57	0.36
	7.07	Herbivore (Broadleaf plants)	16.13	**2.3**	11.94	**1.7**	5.33	0.75	3.95	0.56

Values in bold indicate RQ>1.
[1] based on the NOEC of 125 mg a.i./kg diet converted to a daily dose using default feeding and bird weight parameters

Table 4b Screening level avian risk assessment based on lowest crop application rate (brassica and leafy vegetables – 34.56 g a.i./ha).

	Toxicity (mg a.i./kg bw/d)	Feeding Guild (food item)	EDE (mg a.i./kg bw)	RQ
Small Bird (0.02 kg)				
Acute	200.00	Insectivore	2.81	0.01
Reproduction	7.07[1]	Insectivore	2.81	0.40
Medium Sized Bird (0.1 kg)				
Acute	200.00	Insectivore	2.20	0.01
Reproduction	7.07	Insectivore	2.20	0.31
Large Sized Bird (1 kg)				
Acute	200.00	Herbivore (short grass)	1.42	0.01
Reproduction	7.07	Herbivore (short grass)	1.42	0.20

[1] based on the NOEC of 125 mg a.i./kg diet converted to a daily dose using default feeding and bird weight parameters

Table 5 Effects of permethrin on freshwater aquatic invertebrates

Organism	Exposure	Test Substance	Endpoint Value[a] (µg a.i./L)	Comments	Reference
Acute					
		Ambush (50% EC formulation)	48-h LC_{50} = **4.0** NOEC = 1.5		
		(Technical)	48-h LC_{50} = **0.6** NOEC = 0.1		
		Technical (95.7%)	48-h LC_{50} = **0.039**		USEPA 2004; - WFD-UKTAG 2012 (PMRA 2677256
		Technical	48-h LC_{50} = **0.32**		USEPA 2004; WFD-UKTAG 2012 (PMRA 2677256; WHO 2011 (PMRA 2677259)
		Technical	48-h LC_{50} = **0.58**		USEPA 2004

Organism	Exposure	Test Substance	Endpoint Value[a] (µg a.i./L)	Comments	Reference
		Technical (94.4%)	48-h LC_{50} – **0.7**		USEPA 2004; WFD-UKTAG 2012 (PMRA 2677256
		Technical (91%)	48-h LC_{50} – **1.26**	Classified as supplemental by EPA.	USEPA 2004; WHO 1990 (PMRA 2677257)
		Technical (95.7%)	48-h LC_{50} – **7.2**		USEPA 2004; WFD-UKTAG 2012 (PMRA 2677256
		25 EC formulation	48-h LC_{50} – **0.76**		USEPA 2004
		25 EC formulation	48-h LC_{50} – **0.58**		USEPA 2004; WFD-UKTAG 2012 (PMRA 2677256
		25 EC formulation	48-h LC_{50} – **1.31**	Classified as supplemental by EPA.	
		26.2% formulation	48-h LC_{50} – **3.3**		
		10 EC formulation	48-h LC_{50} – **9.9**		
		Form of test substance not reported	48-h EC_{50} – **0.112**		
		EC formulation (25.6%)	48-h LC_{50} – **1.25**	Neonates < 24 hours. Static conditions. LC_{50} determined based on nominal concentrations.	
	Acute 96-h	Technical (99.3%)	96-h LC_{50} – **0.65** (control – DOM free) 96-h LC_{50} – **0.57 – 1.00** (DOM treatment groups)	The potential of low concentrations of dissolved organic matter (DOM: 3 – 20 mg/L) in natural surface waters to inhibit permethrin acute toxicity was investigated. The presence of DOM did not appear to significantly decrease permethrin uptake or increased its LC_{50} value.	Yang *et al.* 2007 – PMRA 2666972
	Acute	Not reported	LC_{50} – **0.11**	Data originates from USEPA Ecotox Database. Given that this acute endpoint falls within the range of other aquatic insect acute endpoints, the value will be considered in the risk assessment.	Davis *et al.*, 2007 – PMRA 2677269
	Acute 48-h	86.6% pure; 40:60 mixture of *cis* and trans isomers	48-h LC_{50} – **1.06** (150 mL volume) 48-h LC_{50} – **0.43** (300 mL volume)	The effect of bioassay volume on the toxicity was investigated. Static conditions. LC_{50} determined based on nominal concentrations.	Stratton and Giles 1990

Organism	Exposure	Test Substance	Endpoint Value[a] (µg a.i./L)	Comments	Reference
	Acute 96-h	Racemic permethrin: 99.4% trans 99.3% cis	96-h LC_{50} = **0.788** (cis) 96-h LC_{50} = **0.738** (trans)	Enantioselectivity in aquatic toxicity was evaluated through 96-h acute toxicity assays. To remain consistent with toxicity values reported in other studies, the LC_{50} values for the racemate will be considered for the risk assessment.	Liu *et al.*, 2005a
	Acute 72-h	EC permethrin (50% v/v active - 40:60 cis/trans)	72-h LC_{50} = **9.20**	Average of three values : 6.8, 7.11 and 13.7 µg a.i./L.	Sibley and Kaushik 1991 PMRA 2666039
		3-phenoxybenzyl alcohol (PBalc)	EC_{50} >50		
		3-phenoxybenzaldehyde (PBald)	EC_{50} >50		
			EC_{50} >50		
			EC_{50} = 89,000		USEPA RED 2005 (PMRA 2350160)
	Acute 96-h	Racemic permethrin: 99.4% trans 99.3% cis	96-h LC_{50} = **0.539** (cis) 96-h LC_{50} = **0.519** (trans)	Enantioselectivity in aquatic toxicity was evaluated through 96-h acute toxicity assays. To remain consistent with toxicity values reported in other studies, the LC_{50} values for the racemate will be considered for the risk assessment.	Liu *et al.*, 2005a
	Acute 48-h	EC formulation (25.6%)	48-h LC_{50} = **0.55**	Neonates <24 hours. Static conditions. LC_{50} determined based on nominal concentrations.	WDF-UKTAG 2012
	Acute 48-h	Technical (99%)	48-h LC_{50} = **0.066**	Neonates <24 hours. Static conditions. LC_{50} determined based on nominal concentrations.	Wheelock *et al.*, 2005 (PMRA 2666878)
	Acute 96-h	^{14}C labelled technical 98% radiopurity	Based on SS free treatment group: 96-h LC_{50} = **0.51** Based on SS treatment groups 25 – 100 mg/L SS: 96-h LC_{50} = **0.61 – 1.1**	*C. dubia* (<24 h old) were exposed to test solutions prepared with different levels of suspended sediment obtained from four sediment sources (0, 25, 50 and 100 mg/L SS). Results of study demonstrated that the effect of suspended solids does not drastically reduce potential permethrin toxicity to pelagic organisms.	Yang *et al.*, 2006a (PMRA 2666881)

Organism	Exposure	Test Substance	Endpoint Value[a] (µg a.i./L)	Comments	Reference
	Acute 96-h	^{14}C labelled technical 98% radiopurity	Based on DOM free treatment group: 96-h LC_{50} = **0.52** Based on DOM treatment groups (1 – 30 mg/L): 96-h LC_{50} = **0.52 – 1.1**	*C. dubia* (< 24 h old) were exposed to test solutions prepared with different levels of dissolved organic matter (DOM: 0 – 30 mg/L). Results of study demonstrated that the effect of dissolved organic carbon does not drastically reduce potential permethrin toxicity to pelagic organisms.	Yang *et al.* 2006b (PMRA 2666879)
Daphnia pulex	Acute 48-h	EC permethrin (50% v/v active - 40:60 cis/trans)	48-h LC_{50} = **6.45**	Geomean of 3 values (2.75, 7.45 and 13.1 µg a.i./L). Cited from Sibley and Kaushik 1991 (PMRA 2666039).	WDF-UKTAG 2012
Scud *Gammarus pseudolimnaeus*	Acute 96-h	Technical (91%)	96-h LC_{50} = **0.17**		
Crayfish *Procambarus blandingii*	Acute 48-h	Technical (89.1%)	48-h LC_{50} = **210**	Classified as supplemental by EPA.	
Red Swamp Crayfish *Procambarus clarkii*	Acute 96-h	EC formulation (25.6%)	Geomeans: 96-h LC_{50} = **0.48** 96-h LC_{50} = **0.84** 96-h LC_{50} = **1.3** 96-h LC_{50} = **0.80**	Static conditions. Endpoints based on nominal concentrations. Size class: 8 – 12mm Size class: 25 – 35mm Size class: 45 – 55mm Size class: 65 – 75mm	
	Acute 96-h	Form of test substance not reported	96-h LC_{50} = **0.34** NOEC = 0.03		
	Acute static renewal	Technical (~99%)	96-h LC_{50} = 0.44 120-h LC_{50} = 0.26 144-h LC_{50} = **0.17**	The LC_{50} values were determined based on measured exposure concentrations. Additional biomarker experiments (ChE and GST activity); significant increases in enzyme activity occurring after 48-h exposure at 0.12 µg/L. Significant reduction in feeding rate was observed at all test concentrations; the concentration of permethrin resulting in 10% change in feeding rate (EC10) for the 144 hours exposure period was 0.009 µg/L.	McLoughlin *et al.*, 2000 (PMRA 2666966)
		Technical (90.8%)	24-h LC_{50} = **0.45**		
		Microencapsulated permethrin (20% purity)	24-h LC_{50} = **21.6**		

Organism	Exposure	Test Substance	Endpoint Value[a] (µg a.i./L)	Comments	Reference
Mosquito larvae *Aedes albopictus*	Acute 24-h	Form of test substance not reported	24-h LC_{50} = **0.95**		
Mosquito larvae *Aedes atropalpus*	Acute 24-h		24-h LC_{50} = **6.168**		
Mosquito larvae *Aedes hendersoni*	Acute 24-h		24-h LC_{50} = **3.504**		
Mosquito larvae *Aedes triseriatus*	Acute 24-h		24-h LC_{50} = **6.62**	Geomean of 6 values (4.46, 6.23, 6.39, 7.38, 7.68 and 8.39).	
Chironomus riparius	Acute 96-h		24-h LC_{50} = 34.4 48-h LC_{50} = 9.27 72-h LC_{50} = 4.62 96-h LC_{50} = **2.89**	Spiked natural sediment (OC = 9.64%). Static conditions. 8 to 10 day old larvae were used. Endpoint based on nominal test concentrations. 24 – 96h values based on same exposure test.	Conrad et al. 1999 (PMRA 2666995); WFD-UKTAG 2012 (PMRA 2677256)
Chironomus thummi	Acute 24-h		24-h LC_{50} = **16.6**		
Great pond snail *Lymnaea stagnalis*	Acute 48-h		48-h LC_{50} = 100000		
Chironomus plumosus	Acute 48-h	Technical (purity not reported)	48-h LC_{50} = **0.56**	3rd instar	WHO 1990 (PMRA 2677257)
Hexagenia bilineata	Acute 96-h	Permethrin (purity not reported)	96-h EC_{50} = **0.1**		EPA 2004, WFD-UKTAG 2012 (PMRA 2677256)
	1-h exposure	Technical (98%)	56 day NOEC = 0.205 µg/L (based on reduced surviving pairs and reproductive output; mean measured)	Pairs (10 week old) were pulse exposed for 1 hour to simulate a realistic run-off event. Acute and delayed effects (pairing behaviour, reproductive output) on precopulatory pairs of *H. azteca* were investigated for 56 days.	Pedersen *et al.*, 2013 (PMRA 2692367)
		Technical (99%)	96-h LC_{50} = **0.036**	Static conditions. LC_{50} determined based on nominal concentrations.	Wheelock *et al.*, 2005 (PMRA 2666878)
		Permethrin (purity not reported)	96-h LC_{50} = **0.021**		

Organism	Exposure	Test Substance	Endpoint Value[a] (µg a.i./L)	Comments	Reference
Chironomus dilutes	Acute 96-h	Permethrin (purity not reported)	96-h LC_{50} = **0.059**	these acute endpoints fall within the range of other aquatic insect acute endpoints, these values will be considered in the risk assessment.	2677605)
Chironomus tentans	Acute, 96-h	Permethrin (purity not reported)	96-h LC_{50} = **10.45**		
Mayfly larvae *Baetis rhodani*	Acute 96-h Flow through	Permethrin (EC; purity not reported)	96-h LC_{50} = **12.0**		
Mayfly larvae *Cloen dipterum* (L); early instar	Acute 72-h Static	Permethrin (purity not reported)	72-h LC_{50} = **0.03**		
Stonefly larvae *Pteronarcys dorsata*	Acute 72-h Flow through	Permethrin (purity not reported)	72-h EC_{50} = **0.15** 72-h LC_{50} > 0.40		
Lesser water boatman (adults) *Corixa punctata* (Illiger)	Acute 24-h Static	Permethrin (purity not reported)	24-h EC_{50} = **0.7** 24-h LC_{50} > 5.0		
Caddisfly larvae *Brachycentrus americanus*	Acute 96-h Flow through	Permethrin (purity not reported)	96-h EC_{50} = **0.4** 96-h LC_{50} > 0.5		
Caddisfly larvae *Hydropsyche californica*	Acute 24-h Intermittent flow through	Permethrin (purity not reported)	24-h $EC_{90.95}$ = 0.1 (1 h exposure period)		
Blackfly *Simulium* spp.	Acute 24-h Intermittent flow through	Permethrin (purity not reported)	24-h LC_{50} = **0.02 – 0.4** (pupae) 24-h LC_{50} = **0.07 – 0.6** (larvae) 24-h LC_{50} = 0.1 (larvae, 1 h exposure) 24-h LC_{50} = 1.0 (larvae, 1 h exposure)		
Glochidia freshwater mussel *Villosa delumbis* and *Villosa constricta*	Acute 48-h static		48-h EC_{50} > **200**	Survival	

Organism	Exposure	Test Substance	Endpoint Value[a] (µg a.i./L)	Comments	Reference
two-month-old juvenile freshwater mussel *L. siliquoidea* and *L. fasciola*	Acute 96-h static renewal		96-h EC_{50} > 200	Survival (based on movement inside or outside of the shell)	
Chronic					
	21 d Chronic Static renewal	Ambush (50% EC formulation)	21 Day MATC = 0.09 21 d NOEC = 0.06	LOEC: Significantly reduced adult daphnid length in comparison with pooled controls.	EFED 2008; (original study PMRA 1155875)
	21 d Chronic	Technical (94%)	21 d NOEC = 0.28 LOEC = 0.56	Reproduction	
	21 d Chronic	Technical (99%)	21 d NOEC = 0.039 LOEC = 0.084	Reproduction and growth	
	21d Chronic Semi static	Technical (93.6%)	21 d NOEC = 0.008 (nominal) 21 d NOEC = **0.0047** (mean)	Reproduction test	WHO 2011 (PMRA 2677259)
	Chronic	Not reported	NOEC = 0.3	The duration of the exposure is not cited. Data originates from USEPA Ecotox Database. The endpoint falls within the range of other chronic aquatic insect chronic endpoints.	Davis *et al.* 2007 (PMRA 2677269)
	40 d static		NOEC = 1 LOEC = 5	Mortality endpoints: =50% mortality observed at LOEC. Exposure concentrations not measured; no analytical procedure to measure the residual concentration of the permethrin microcapsule formulation in aqueous media has been developed. Exposure conditions were static (because of the slow release nature of the microcapsules). Cited from Sibley and Kaushik (PMRA 266039)	
D. pulex	32 d static		NOEC = 1 LOEC = 1	Mortality endpoints: =90% mortality observed at LOEC. Exposure concentrations not measured; no analytical procedure to measure the residual concentration of the permethrin microcapsule formulation in aqueous media has been developed. Exposure conditions were static (because of the slow release nature of the microcapsules). Cited from Sibley and Kaushik (PMRA2666039)	
Caddisfly larvae *Brachycentrus americanus*			21 d LC_{50} = 0.17 28 d NOEC = 0.03	Mortality; LOEC = 0.03 µg a.i./L; at this concentration more than 55% mortality was observed after 28 days.	WFD-UKTAG 2012 (PMRA 2677256); WHO 1990 (PMRA 2677257)

Organism	Exposure	Test Substance	Endpoint Value[a] (µg a.i./L)	Comments	Reference
Stonefly larvae *Pteronarcys dorsata*			21 d EC_{100} = 0.042 28 d NOEC = 0.029	Within 2 hours, 25% of the animals were immobilised upon exposure to >0.21 µg/L (90% after 5 hours). At 0.12 µg/L, 65% were immobile after 96 hours.100% immobilization ater 21 days.	WFD-UKTAG 2012 (PMRA 2677256)
Mayfly *Hexagenia rigida*	8 weeks	Not reported	0.15 (21% mortality)	Life stage not reported. Treatment related mortality during 8 weeks observation in clean water ager 6 hours exposure to 0.15 µg a.i./L. The WDF-UKTAG 2012 review offers very few details about the study but considers the study reliable.	
Snail *Helosoma trivolvis*	28 days (flow-through)	Permethrin (92%)	>0.33	Snails: individuals of 0.09–0.3 g weight. Snail survival was not significantly decreased up to the highest concentration tested for 28 days (0.33 µg l-1). Snails exposed to the highest concentration responded more slowly when probed than snails exposed to lower concentrations. However, this condition disappeared after the first week of exposure.	
	20-d	Nominal concentrations (mg/kg) of 0 (control), 0.2, 0.4, 0.8 and 1.6.	NOEC = 0.4 mg/kg mg a.i./kg dry weight sediment	NOEC based on emergence of adults. Spiked natural sediment (OC = 1.23%). At 0.8 mg/kg, 63% reduction of emergence compared with controls.	
	10-d	Form of test substance not reported	LC_{50} = 2.11 mg a.i./kg dry weight sediment	Spiked natural sediment (OC = 9.64%). Static conditions. 8 to 10 day old larvae were used. Endpoint based on nominal test concentrations.	Conrad *et al.* 1999 (PMRA 2666995); WFD-UKTAG 2012 (PMRA 2677256)
	10-d	Permethrin (purity not reported)	LC_{50} = 0.235 mg a.i./kg dry weight sediment	Exposure to spiked sediments.	Chen *et al.*, 2015 – PMRA 2666904
			10-d LC_{50} = 1.1 µg/L		
			10-d LC_{50} = 0.86 µg/L		
	10-d	Technical (20% cis, 78% trans)	LC_{50} = 0.09 mg a.i./kg dry weight sediment	The 10 day LC_{50} value is representative of an average based on tests conducted in three different sediments; individual values were reported as 112, 57 and 102 ng/g dry sediment.	Amweg *et al.* 2005 – PMRA 2666053

a Acute endpoints in bold were used to determine HC_5 values (the 5th percentile of the species sensitivity distribution for the LC_{50} at 50% confidence intervals); geomean values were used for species with multiple endpoint values. The acute HC_5 = 0.019 µg a.i./L. An insufficient number of suitable species endpoints was available to derive a chronic HC_5 value; the chronic endpoint (in bold) is representative of the most sensitive endpoint.

Table 6 Effects of permethrin on fish

Organism	Exposure	Test Substance	Endpoint Value[a] (µg a.i./L)	Comments	Reference
Acute					
			96-h LC_{50} = **0.9** NOEC = 0.68 (mortality)		European Union 1998; PMRA 2431487
			96-h LC_{50} = **0.79**	Listed as supplemental; no rationale provided. Also cited in Davis *et al.* 2007.	
		Permethrin (95.7% purity)	96-h LC_{50} = **2.52**		
		Permethrin (100% purity)	96-h LC_{50} = **6.1**		
		Permethrin (95.7% purity)	96-h LC_{50} = **6.8**	Listed as supplemental; no rationale provided.	
		Permethrin (94.4% purity)	96-h LC_{50} = **13.3**		
		Permethrin (91.4% purity)	96-h LC_{50} = **13.5**		
		Permethrin (91% purity)	96-h LC_{50} = **5.0**		
		24EC	96-h LC_{50} = **10.8**	Listed as supplemental; no rationale provided.	EPA 2004
		24EC	96-h LC_{50} = **13**		EPA 2004
		10EC	96-h LC_{50} = **24**		EPA 2004
		Permethrin (38.5% purity)	96-h LC_{50} = **9.0**		EPA 2004
		Permethrin (purity not reported)	96-h LC_{50} = **33.4**		WDF-UKTAG 2012
	Acute, 96-h	3-phenoxybenzoic acid	96-h LC_{50} = 36,300		USEPA RED 2005 (PMRA 2350160)

Organism	Exposure	Test Substance	Endpoint Value[a] (µg a.i./L)	Comments	Reference
Rainbow trout *(Oncorhynchus mykiss)*	Acute, 96-h	Ambush (50% EC formulation)	96-h LC_{50} = **4.5** NOEC = 0.83		European Union 1998; PMRA 2431487
		Permethrin (95% purity)	96-h LC_{50} = **9.8**		
		Permethrin (94% purity)	96-h LC_{50} = **5.3**	Listed as supplemental; no rationale provided.	
		Permethrin technical	96-h LC_{50} = **2.1**	Listed as supplemental; no rationale provided.	
		Permethrin (91% purity)	96-h LC_{50} = **2.9**		
		24EC	96-h LC_{50} = **56**	Listed as supplemental; no rationale provided.	
		26.2% purity	96-h LC_{50} = **32**		
		10.6% purity	96-h LC_{50} = **73**		
		Permethrin (purity not reported)	96-h LC_{50} = 0.014	Flow through test design. WFD-UKTAG 2012 states that result is given as µg/L but may be µmol/L, which equals 5.5 µg/L, which would then agree with other *O. mykiss* acute mortality data. Based on this uncertainty, the endpoint is not considered for the risk assessment.	
		Permethrin (purity not reported)	96-h LC_{50} = **20.9**		
		Permethrin (purity not reported)	96-h LC_{50} = **5.5**		
		Permethrin (purity not reported)	96-h LC_{50} = **3.3**	Juveniles; ca. 0.2–1 g bw. Static conditions. (Reported in Dwyer *et al.* 2005a – PMRA 2671948)	
			96-h LC_{50} = **0.62**	1 g, flow through, 5°C	
			96-h LC_{50} = **0.69**	1 g, flow through, 10°C	
			96-h LC_{50} = **3.2**	1 g, flow through, 15°C	
			96-h LC_{50} = **6.4**	5 g, flow through, 15°C	
			96-h LC_{50} = **50**	20 g, flow through, 15°C	
			96-h LC_{50} = **287**	50 g, flow through, 15°C	
			96-h LC_{50} = **314**	200 g, flow through, 15°C	
			96-h LC_{50} = **135**	6 cm, 3 g, 10°C	
		EC	96-h LC_{50} = **61**	6 cm, 3 g, 10°C	

Organism	Exposure	Test Substance	Endpoint Value[a] (µg a.i./L)	Comments	Reference
		EC	48-h LC_{50} – **6.0**	5 – 6 cm, 12 °C	
		EC (cis)	48-h LC_{50} – 7.0	5 – 6 cm, 25.5 °C. Value not considered in risk assessment (temperature not relevant for this species – 10 – 14°C).	
		Permethrin technical	24-h LC_{50} – **18**	2 – 4 g, Static, 12 °C	
		cis	24-h LC_{50} – **25**	2 – 4 g, static, 12 °C	
		trans	24-h LC_{50} – **14**	2 – 4 g, static, 12 °C	
		3-phenoxybenzoic acid	96-h LC_{50} – 13,300		PMRA 1160907 1239776, EPA RED (PMRA 2350160)
		Cis trans DCVA	96-h LC_{50} – 3100		PMRA 1160907
		Permethrin (92.5% purity)	96-h LC_{50} – **3.2**		
		Permethrin Technical	96-h LC_{50} – **3.9**	Listed as supplemental; no rationale provided.	
		5.7% purity	96-h LC_{50} – **5.2**	Listed as supplemental; no rationale provided.	
		13EC	96-h LC_{50} – **2.3**	Listed as supplemental; no rationale provided.	
		Permethrin (91% purity)	96-h LC_{50} – **5.7**		
			96-h LC_{50} – **3.0**		USEPA 2004, WED-UKTAG 2012 (PMRA 2677256)
			96-h LC_{50} – **9.4**	(Reported in Dwyer *et al.* 2005a – PMRA 2671948)	
		Permethrin (purity not reported)	96-h LC_{50} – **16**		
		Permethrin (purity not reported)	96-h LC_{50} – **62.6**		
		Permethrin (91% purity)	96-h LC_{50} – **7.2**		
		Permethrin technical	96-h LC_{50} – **5.4**		
		EC	96-h LC_{50} – **1.1**	1.4 – 1.7 cm (0.02 g), static, 24°C	

Organism	Exposure	Test Substance	Endpoint Value[a] (µg a.i./L)	Comments	Reference
Largemouth bass *Micropterus salmoides*	Acute 96-h	EC	96-h LC_{50} = **8.5**	4.5 – 5.5 cm, (1.14 g), static, 24°C	2677257)
	Acute, 96-h	Technical (94.1%)	96-h LC_{50} = **8.9**		WHO 2011 (PMRA 2677259)
	Acute, 48-h	Technical (94.9%)	48-h LC_{50} = **245.7** (nominal)	Note: A much lower 96 hour LC_{50} value is reported for *P. reticulata* in the WHO 2011 review for permethrin (above). Had the exposure duration used in the study been extended to 96 hours, the LC_{50} value may have been lower.	Başer S. *et al.* 2003 PMRA 2671873
White sucker *Catostomus commersoni*	Acute, 2-h	Permethrin (94.4% purity)	96-hour LC_{50}: Larvae - 13 days old: 184 µg/L (fed), 2.0 µg /L (unfed) Larvae - 20 days old: 10 µg/L (fed), 1.0 µg/L (unfed) Larvae - 26 days old: 3668 µg /L (fed), 172 µg/L (unfed)	Larvae, 13, 20 or 26 days old. Fed or unfed during 2 hours of exposure and subsequent 94-hour observation period. (mortality observed after 2-hour pulse exposure plus 94-hour observation time) Value not considered in risk assessment, (exposure duration too short – 2h).	
	Acute, 96-h	Permethrin (purity not reported)	96-h LC_{50} = **8.7**	Geomean of two values (6.3 and 12 µg a.i./L).	
	Acute, 96-h	EC	96-h LC_{50} = **15**	1.5 – 2.5 cm, static 24°C	
	Acute, 48-h	EC	48-h LC_{50} = **97**	4 – 5 cm, 9 – 16°C	
Lahontan cut-throat trout *Oncorhynchus clarkihenshawi*	Acute, 96-h		96-h LC_{50} = **1.6**		
Greenback cut-throat trout *Oncorhynchus clarki stomias*	Acute, 96-h		96-h LC_{50} = **1.0**		
Apache trout *Oncorhynchus gilae apache*	Acute, 96-h		96-h LC_{50} = **1.7**		
	Acute, 48-h	Technical (+) – trans (+) – *cis* (-) trans (-) - cis	48-h LC_{50} = **41** 48-h LC_{50} = **17** 48-h LC_{50} = **13** 48-h LC_{50} = 10000 48-h LC_{50} = 10000	Static, 25°C, adult.	WHO 1990 (PMRA 2677257)

Organism	Exposure	Test Substance	Endpoint Value[a] (µg a.i./L)	Comments	Reference
	Acute, 48-h, static renewal	Permethrin (88%)	48-h LC_{50} = **11**	30-day-old japanese medaka. Endpoint based on measured test concentrations.	Rice J.R. *et al.*, 1997 (PMRA 2677604)
Desert pupfish *Cyprinodon macularis*	Acute, 48-h	EC	48-h LC_{50} = **5**	4 – 5 cm, static, 11 – 17°C	
Tilapia mossambica	Acute, 48-h	EC	48-h LC_{50} = **44**	5 – 6 cm, static, 15 – 21°C	
Bleak *Alburnus alburnus*	Acute, 96-h	EC	LC_{50} = **4 - 8**	8 cm; static conditions, 10°C pH 7.8, 7‰	
Spotfin chub *Erimonax monachus*	Acute, 96-h	Permethrin (purity not reported)	96-h LC_{50} = **1.7**		
Greenthroat darter *Etheostoma lepidum*	Acute, 96-h	Permethrin (purity not reported)	96-h LC_{50} = **2.71**		
Cape Fear Shiner *Notropis mekistocholas*	Acute, 96-h	Permethrin (purity not reported)	96-h LC_{50} = **4.16**		
Razorback sucker *Xyrauchen texanus*	Acute, 96-h	Permethrin (purity not reported)	96-h LC_{50} = **5.95**		
Colorado pikeminnow *Ptychocheilus lucius*	Acute, 96-h	Permethrin (purity not reported)	96-h LC_{50} = **24**		
Elephant fish *Poilumyrus isidori*	Acute 48-h static renewal	Permethrin (purity not reported)	48-h LC_{50} = **26**	Limited details are provided for methodology. The authors also report a 72 hour LC_{50} of 20 µg/L; this value appears to have been extrapolated from a toxicity curve (time versus LC_{50} concentration); however, the method of curve fitting is unclear.	Yameogo L., *et al.*, 1991 (PMRA 2678872)
Nile tilapia *Oreochromis niloticus*			48-h LC_{50} = 27		
Redbelly tilapia *Tilapia zillii*			48-h LC_{50} = **49**		
Indian major carp *Labeo rohita*	Acute 96-h	Permethrin (purity not reported)	96-h LC_{50} = **3.05**	The 96 hour LC_{50} endpoint is from another study; the source of the 96 hour LC_{50} value is not cited. The reviewer assumes it was derived from previous toxicity tests that are not published. The endpoint value falls within the range of 96 hour LC_{50} values reported for other fish species; this endpoint will be taken at face value and considered in the risk assessment.	Nayak A.K., *et al.* 2004 (PMRA 2671874)

Organism	Exposure	Test Substance	Endpoint Value[a] (µg a.i./L)	Comments	Reference
Shortnose sturgeon *Acipenser brevirostrum*	Acute 96-h	Technical (95.2%)	96-h LC_{50} = 1.2		Dwyer *et al.* 2005a. (PMRA 2671948)
Bonytail chub *Gila elegans*			96-h LC_{50} = **25**		
Fountain darter *Etheostoma fonticola*			96-h LC_{50} = **3.34**		
Gila topminnow *Poeciliopsis occidentalis*			96-h LC_{50} = **10.0**		
Brook trout *Salvelinus fontinalis*	Acute 96-h	Technical (~92%)	96-h LC_{50} = **2.86**	The endpoints are based on nominal test concentrations.	Paul E. A. *et al.*, 2005 (PMRA 2671952)
		Technical (90%)	96-h LC_{50} = **2.5**		Zhang Z-Y. *et al.*, 2010 (PMRA 2677589)
		Permethrin (purity not reported)	96-h LC_{50} = **0.13**	The toxicity endpoint is based on nominal test concentrations.	Tiwari P., *et al.*, 2014 (PMRA 2677606)
	Acute 48-h static	Permethrin (purity not reported)	48-h LC_{50} = **20**	Toxicity test was conducted with zebrafish embryos 24 hours post fertilization. The toxicity endpoint is based on nominal test concentrations.	Knöbel M., *et al.*, 2012 (PMRA 2677593)
	Acute 120-h static renewal	Technical (98.3%)	120-h LC_{50} = **467.5**	The toxicity endpoint is based on nominal test concentrations.	Yang Ye, *et al.*, 2014 (PMRA 2677598)
	Acute 144-h static	Technical (46% cis, 52% trans)	144-h LC_{50} = **300**	The toxicity endpoint is based on nominal test concentrations.	Demicco A. *et al.*, 2010 (PMRA 2671954)
Common carp *Cyprinus carpio*	Acute, 24-h static	Permethrin (25EC, 25g a.i./L)	24-h LC_{50} = **35**	Fry of Cyprinus carpio (4 ± 0.3 cm, 2 ± 0.2 g) were exposed to five nominal different concentrations of permethrin for 24 hours under static conditions. LC_{50} reported as 35.37ppm (35 µg/L based on nominal concentration of the actual aquarium water).	Sial I.M. *et al.*, 2009 (PMRA 2677239)
Chronic					
Rainbow trout *Oncorylnchus mykiss*	21-d	Ambush (50% EC formulation)	MATC = 2.2 NOEC = 0.42	Study duration 21 days; the nature of the study is not reported.	European Union 1998; PMRA 2431487
Zebra fish *Danio rerio*	35-d ELS	Technical (93.6%)	NOEC = 0.41	Dosage: 0.06, 0.13, 0.25, 0.50 and 1.00 µg/L.	WHO 2011 (PMRA 2677259)

Organism	Exposure	Test Substance	Endpoint Value[a] (µg a.i./L)	Comments	Reference
Fathead minnow *Pimephales promelas*	ELS 32-d (flow-through)	Permethrin (92%)	NOEC = 0.66	Fish: 4–5-day-old larvae. Significantly reduced survival and impaired swimming ability at a concentration of 1.4 µg I/L. One day after hatch, survival of larvae at this concentration was reduced to 37%. Most larvae that survived were convulsive. Four days after hatch, only one larva remained alive at 1.4 µg/L. No significant effects on survival were seen at permethrin concentrations of 0.66 µg I/L or less. Hatchability, normal appearance and growth of embryos were not decreased at any concentration tested after the 32-day test.	WFD-UKTAG 2012 (PMRA 2677256)
	Full life cycle	Permethrin (purity not reported)	NOEC = 0.30 LOEC = 0.41	Full life cycle exposure resulted in significant reduction in number of fry surviving to 30 days. No Effect on growth or number of eggs produced.	USEPA EFED 2006 (PMRA 2431484)

a – Acute endpoints in bold were used to determine HC_5 values (the 5th percentile of the species sensitivity distribution for the LC_{50} at 50% confidence intervals); geomean values were used for species with multiple endpoint values. The acute HC_5 = 1.2 µg a.i./L. An insufficient number of suitable species endpoints was available to derive a chronic HC_5 value; the chronic endpoint (in bold) is representative of the most sensitive endpoint.

Table 7 Effects of permethrin on amphibians

Organism	Exposure	Test Substance	Endpoint Value (µg a.i./L)	Comments	Reference
			LC_{50} = 115		WFD-UKTAG 2012 (PMRA 2677256)
			LC_{50} = 7033	Tadpoles were 0.6 – 0.8 cm, toxicity tests were conducted at 24°C under static conditions.	WHO 1990 (PMRA 2677257)
Boreal toad *Bufo boreas boreas*		Technical (95.2%)	LC50 > 10	Based on nominal test concentrations. Age of toads not reported.	Dwyer *et al.* 2005a (PMRA 2671948)
Common frog *rana temporaria* tadpoles	Acute, 72 h	Permethrin (purity not reported)	LC_{50} = 2	Based on nominal test concentrations.	Johansson M., *et al.*, 2006 – PMRA 2677268
Green frog *Rana clamitans* tadpoles	Acute, 96 h	Technical (99%)	NOEC = 10 (mortality)	Tadpoles (Gosner stage 25). Based on nominal test concentrations.	Puglis H.J., and M.D. Boone. 2011 (PMRA 2677590)

Table 8 Effects of permethrin on freshwater algae and vascular plants

Organism	Exposure	Test Substance	Endpoint Value (mg a.i./L)	Comments	Reference
Algae					
	Acute, 96 h static	Permethrin (95%)	EC_{50} = 12.5 NOEC = 0.87		
	Acute, 96 h static	Ambush (50% EC formulation)	EC_{50} = 61 NOEC = 1.6		
	Acute, 72 h static	Permethrin (~96% purity)	EC_{50} >160 NOEC = 160	Growth rate and biomass	
Green algae *Chlamydomonas reinhardtii*	Acute, 72 h static	Permethrin (93% purity)	NOEC = 4700	Inhibition of cell growth (in percentage of cell number of control).WFD-UKTAG 2012 reports the following: EC0 is 4.7 mg/L, EC100 = 391 mg/L. From Figure 1 of the publication, an EC10 of 5.1 mg/L can be inferred. No description of growth medium, no measurement of toxicant concentrations in test.	

Organism	Exposure	Test Substance	Endpoint Value (mg a.i./L)	Comments	Reference
Green algae *Chlorella pyrenoidosa*	Acute	Technical (purity not reported)	EC_{50} – 10000	Growth rate and biomass Optical densities of treated cultures (cell yield) were determined daily for 12 to 14 days and per cent inhibition values were calculated relative to control systems. The EC_{50} is assumed to be based on a 12 day period.	WHO 1990 (PMRA 2677257); Stratton and Corke 1982 (PMRA 2677249)
Green algae *Scenedesmus quadricaudata*			EC_{50} – 10000		
Blue- green algae *Anabaena inaequalis*			EC_{50} – 1600 (growth rate) EC_{50} – 5000 (biomass)		
Vascular plants					
No toxicity data for freshwater aquatic plants is available.					

Table 9 Effects of permethrin on marine invertebrates

Species	Test substance	Endpoint observed	Value[a] (µg a.i./L)	Comments	Reference
Acute					
			LC_{50} – **0.019**	Listed as supplemental, i.e. study is scientifically sound, but does not satisfy guideline	USEPA 2004
			LC_{50} – **0.046**	Listed as supplemental, i.e. study is scientifically sound, but does not satisfy guideline. 1 day old; static, 25°C, 20 ‰.	USEPA 2004; WHO 1990 (PMRA 2677257)
			LC_{50} – **0.02**	Listed as supplemental (i.e. study is scientifically sound, but does not satisfy guideline). Flow-through test design.	USEPA 2004; WFD-UKTAG 2012 (PMRA 2677256)
	Permethrin (90.8% purity)		LC_{50} – **0.075**		USEPA 2004; WFD-UKTAG 2012 (PMRA 2677256)
			LC_{50} – **0.095**	24-hour-old postrelease juveniles. Static conditions.	
			LC_{50} – **0.02**		
	10EC		LC_{50} – **0.47**		USEPA 2004
	Technical (97.7%)		LC_{50} – **0.14**	Juvenile stage (7-day-old mysids). Static renewal conditions.	Delorenzo *et al.* 2014 (PMRA 2667078)
	Permethrin (purity not reported)		LC_{50} – **0.15**		Clark J.R., *et al.* 1989 (PMRA 2677600)
	EC		LC_{50} – **0.6**	3 – 6 weeks old; static conditions, 20 – 22°C pH 7.8, 7‰.	WHO 1990 (PMRA 2677257)
Brown Shrimp *(Penaeus aztecus)*	Permethrin (89% purity)		LC_{50} – **0.34**		WHO 1990 (PMRA 2677257); WFD-UKTAG 2012 (PMRA 2677256)
	Permethrin		LC_{50} – **0.22**	Listed as supplemental by USEPA, i.e. study is scientifically sound, but does not	USEPA 2004; WFD-UKTAG

Species	Test substance	Endpoint observed	Value[a] (µg a.i./L)	Comments	Reference
(Penaeus duorarum)	(93% purity)			satisfy guideline. Flow-through test design. Adult; 25°C, 25 ‰.	2012 (PMRA 2677256); WHO 1990 (PMRA 2677257)
	Permethrin (95.7% purity)		LC_{50} = **0.35**		
	40.6% purity		LC_{50} = **0.51**		
	Permethrin (purity not reported)		LC_{50} = **0.17**	3–5-day-old postlarvae. Static conditions.	WFD-UKTAG 2012 (PMRA 2677256)
	Permethrin (95.7% purity)		LC_{50} = **2.39**		
	Permethrin (89% purity)		LC_{50} = **2.65**	Listed as supplemental, i.e. study is scientifically sound, but does not satisfy guideline	
	40.67% purity		LC_{50} = **7.6**		
	Permethrin (purity not reported)		LC_{50} = **2.2**		Clark J.R., *et al.* 1989 (PMRA 2677600)
Fiddler crab *(Uca pugnax)*	Permethrin (60% trans, 40% cis; Biomist product label – purity not reported)		LC_{50} > 8965 µg kg (dry weight sediment)	Sediment exposure. Hepatopancreas GST was significantly increased at all test concentrations (NOEC = 100 µg/kg sediment.	Stueckle *et al.* 2008 (PMRA 2667057)
Stone Crab *(Menippe mercenaria)*	Permethrin (93% purity)		LC_{50} = **0.018**	Listed as supplemental, i.e. study is scientifically sound, but does not satisfy guideline. Zoea larva; static, 25°C, 20 ‰.	USEPA 2004, WHO 1990 (PMRA 2677257)
	Permethrin technical (purity not reported)		EC_{50} = **1050**	Shell deposition. Listed as supplemental By USEPA, i.e. study is scientifically sound, but does not satisfy guideline	USEPA 2004; WFD-UKTAG 2012 (PMRA 2677256)
	10EC		LC_{50} = **6500**		
			LC_{50} > **536**	Listed as supplemental, i.e. study is scientifically sound, but does not satisfy guideline	
			LC_{50} > **407**	Listed as supplemental, i.e. study is scientifically sound, but does not satisfy guideline	
	Permethrin (95.7% purity)	Acute, 48 h	EC_{50} = **1000**	Listed as supplemental by USEPA, i.e. study is scientifically sound, but does not satisfy guideline. Larvae 2 hours old; static conditions, 25°C, 20 ‰; EC_{50} - abnormal development. (also reported in Clark J.R., *et al.* 1989)	USEPA 2004; WHO 1990 (PMRA 2677257)
Shrimp *Crangon septemspinosa*	Permethrin technical (purity not reported)	Acute, 96 h	LC_{50} = **0.13**	1.3 g; Static renewal, 10°C.	WFD-UKTAG 2012 (PMRA 2677256); WHO 1990 (PMRA 2677257)

Species	Test substance	Endpoint observed	Value[a] (µg a.i./L)	Comments	Reference
Lobster *Homerus americanus*	Permethrin technical (purity not reported)	Acute, 96 h	LC_{50} = **0.73**	450 g; Static renewal, 10°C, 30 ‰ (also reported in Clark J.R., *et al.* 1989)	WHO 1990 (PMRA 2677257)
	Permethrin technical (purity not reported)	Acute, 96 h static renewal	Embryo LC_{50} = **6.4** Larval LC_{50} = **0.05** Adult LC_{50} = **0.21**	96 hour acute toxicity to embryonic, larval and adult grasss shrimp under aqueous static renewal conditions.	Delorenzo *et al.* 2006 (PMRA 2667080)
	Technical (~97.7%)	Acute, 96 h static renewal	Larval LC_{50} = **0.05** Adult LC_{50} = **0.11**		Delorenzo *et al.* 2014 (PMRA 2667078)
	Permethrin (purity not reported)	Acute 48 h	LC_{50} = **0.55 – 1.91**	Acute toxicity were conducted female ovigerous grass shrimp collected from four different locations in Chesapeake Bay and one on the outer Atlantic coast. Individual LC_{50} values for each of the populations were 1.91, 0.60, 0.73 and 0.55 µg a.i./L.	Marshalonis *et al.* 2006 (PMRA 2667082)
Queen conch larvae *Strombus gigas*	Permethrin (purity not reported)	Acute 48 h	NOEC = 0.84 LOEC = 4.68 (increased metamorphic success)	Exposure for 12 hours to permethrin followed by 3 hour exposure to algae (*L. potet*) extract (a natural metamorphic inducer for queen conch). Mortality and metamorphic success was recorded at 15 and 48 hours (3 and 36 hours after extract addition). The LOEC (4.68 µg/L - increased metamorphosis success is the measured concentration at time zero of the 7.5 µg/L nominal concentration), the corresponding measured concentration at 12 hours was 0.33 µg/L, the LOEC is an underestimate of this sublethal effect. The NOEC was determined by the reviewer based on visual inspection of the data.	Delgado *et al.* 2013 (PMRA 2667058)
Chronic					
Mysid shrimp	Permethrin (purity not reported)	30 day life cycle	NOEC = 0.011 LOEC 0.024	Mortality	EPA 2004

a – Acute endpoints in bold were used to determine HC_5 values (the 5th percentile of the species sensitivity distribution for the LC50 at 50% confidence intervals); geomean values were used for species with multiple endpoint values. The acute HC_5 = 0.002 µg a.i./L.

Table 10 Effects of permethrin on marine fish

Species	Test substance	Endpoint observed	Value[a] (µg a.i./L)	Comments	Reference
Acute					
Atlantic silverside (*Menidia menidia*)		Permethrin technical (93% purity)	LC_{50} = **2.2**	Listed as supplemental by USEPA. (i.e. study is scientifically sound, but does not satisfy guideline). Flow-through test design. Adult; 26°C, 25‰.	EPA 2004; WFD-UKTAG 2012 (PMRA 2677256); WHO 1990 (PMRA 2677257)
		Permethrin technical (purity not reported)	LC_{50} = **6.2**		
		Permethrin technical (93% purity)	LC_{50} = **6.6**	Listed as supplemental. (i.e. study is scientifically sound, but does not satisfy guideline).	

Species	Test substance	Endpoint observed	Value[a] (µg a.i./L)	Comments	Reference
		Permethrin technical (93% purity)	LC_{50} = **27.5**	Hemmer M.J., *et al.*, 1992 (original study PMRA 2677237).	WFD-UKTAG 2012 (PMRA 2677256)
		Permethrin technical (93% purity)	LC_{50} = **7.8**	Listed as supplemental by USEPA (i.e. study is scientifically sound, but does not satisfy guideline). Flow-through test design. Adult; 30°C, 22‰.	USEPA 2004; WFD-UKTAG 2012 (PMRA 2677256); WHO 1990 (PMRA 2677257)
		Permethrin (99% purity)	LC_{50} = **17**	Juveniles; ca. 0.2–1 g bw. Static conditions. Saltwater 20‰.	WFD-UKTAG 2012 (PMRA 2677256)
		Permethrin technical (93% purity)	LC_{50} = **88**	Listed as supplemental. (i.e. study is scientifically sound, but does not satisfy guideline). 28-day fry; static, 25°C, 20‰	USEPA 2004; WHO 1990 (PMRA 2677257)
		10EC (purity not reported)	LC_{50} > **300**	Listed as supplemental. (i.e. study is scientifically sound, but does not satisfy guideline).	
Stripped mullet (*Mugil cephalus*)		Permethrin technical (93% purity)	LC_{50} = **5.5**	Listed as supplemental. (i.e. study is scientifically sound, but does not satisfy guideline). Juveniles; flow-through conditions, 24°C, 19‰.	
Coho salmon (*Oncorhynchus kisutch*)			LC_{50} = **17**		
			LC_{50} = **1.5**		
			LC_{50} = **12**		WHO 1990 (PMRA 2677257)
Topsmelt (*Atherinops affinis*)		Permethrin (93% purity)	LC_{50} = **25.3**	Hemmer M.J., *et al.*, 1992 (original study PMRA 2677237).	
Leon Springs pupfish (*Cyprinodon bovinus*)		Permethrin (99% purity)	LC_{50} = **21**	Juveniles; ca. 0.2–1 g bw. Static conditions. Saltwater 2‰.(Reported in Dwyer et al. 2005a – PMRA 2671948)	
Atlantic sturgeon *Acipenser oxyrinchus*	Acute, 96 h	Permethrin (95.2% purity)	LC_{50} = 1.2		Dwyer F.J. *et al.* 2005a (PMRA 2671948)
Juvenile red drum *Sciaenops ocelatus*			LC_{50} = **8.53** NOEC = 3.7 LOEC = 11.1		
Adult mummichop *Fundulus heteroclitus*			LC_{50} = **22.92** NOEC = 11.1 LOEC = 33.3		

Species	Test substance	Endpoint observed	Value[a] (µg a.i./L)	Comments	Reference
Chronic					
Sheepshead minnow *(Cyprinodon variegatus)*	28-d ELS (intermittent flow)	Permethrin (purity not reported)	USEPA: NOEC = 0.83 LOEC = 10.0 WFD-UKTAG: NOEC = 10 (fry survival at 10 µg/L was 99%) LOEC = 22 (fry survival at 22 µg/L was 1%)	The study used 1.5–24-hour-old embryos. Sea water with a salinity ranging from 22–32‰. Endpoints based on measured concentrations. Listed as supplemental by USEPA. The NOEC was = 10 µg a.i./L (based on reduced survival). The EPA states "The estuarine marine chronic value (NOEC = 0.83) is extrapolated by using an acute chronic ratio method of available data from similar species (0.79/0.30 : 2.2/X = 0.83 ppb). (Hansen *et al.* 1983)	EPA 2004, WFD-UKTAG 2012 (PMRA 2677256)

a = Acute endpoints in bold were used to determine HC_5 values (the 5th percentile of the species sensitivity distribution for the LC50 at 50% confidence intervals); geomean values were used for species with multiple endpoint values. The acute HC_5 = 2.38 µg a.i./L.

Table 11 Effects of permethrin on marine algae

Organism	Exposure	Test Substance	Endpoint Value (µg a.i./L)	Comments	Reference
		Not reported	EC_{50} = 68	Growth inhition. Static conditions (22 ± 2°C, pH 8.1 and sea water walinity of 30 ‰). Also reported in Delorenzo and Fulton 2012 (PMRA 2677592).	WFD-UKTAG 2012 (PMRA 2677256)
		Technical	EC_{50} = 92	Growth inhibition. 20°C Also reported in Delorenzo and Fulton 2012 (PMRA 2677592).	WHO 1990 (PMRA 2677257)
			EC_{50} = 72		
			EC_{50} = 124		
Green algae *Dunaliella tertiolecta*			EC_{50} = 104		

Table 12 Summary of screening level risk of permethrin to aquatic organisms

Organism	Exposure	Species	Endpoint reported (µg a.i./L)	Endpoint for RA* (µg a.i./L)	EEC** (µg a.i./L)	RQ	LOC Exceeded
Freshwater							
	Acute	HC_5 (25 species)	HC_5 = 0.019	0.019		**4247**	Yes
	Chronic	Daphnid (*Daphnia magna*)	NOEC = 0.0047	0.0047		**17170**	Yes
	Acute	HC_5 (30 species)	HC_5 = 1.2	1.2		**67**	Yes
	Chronic	Fathead minnow (*Pimephales promelas*)	Full life cycle NOEC = 0.3	0.3		**269**	Yes
	Acute	Common frog tadpoles (*Rana temporaria*)	72 h LC_{50} = 2.0	0.2		**2150**	Yes
	Chronic	Surrogate fish: Fathead minnow (*Pimephales promelas*)	Full life cycle NOEC = 0.3	0.3		**1433**	Yes
Algae	Acute	Green algae (*Pseudokirchneriella subcapita*)	96 h EC_{50} = 12.5	6.25	80.7	**13**	Yes
Marine and estuarine							
	Acute	HC_5 (10 species)	HC_5 = 0.002	0.002		**40350**	Yes
	Chronic	Mysid shrimp	NOEC = 0.011	0.011		**7336**	Yes
Algae	Acute	Diatom *Skeletonema costatum*	EC_{50} = 68	34		**2.4**	Yes
	Acute	HC_5 (10 species)	HC_5 = 2.38	2.38		**34**	Yes
	Chronic	Sheepshead minnow (*Cyprinodon variegatus*)	28 d ELS NOEC = 0.83	0.83		**97**	Yes

* Endpoints used in the acute exposure risk assessment (RA) are derived by dividing the EC_{50} or LC_{50} from the appropriate laboratory study by a factor of two (2) for aquatic invertebrates and plants, and by a factor of ten (10) for fish and amphibians. The HC_5 is the 5th percentile of the species sensitivity distribution for the LC_{50} or NOEC at 50% confidence intervals.
** EEC based on a 15 cm water body depth for amphibians and a 80 cm water depth for all other aquatic organisms.
Bolded values indicates an exceedence of the level of concern (RQ = 1).

Table 13 Spray drift risk assessment for non-target aquatic organisms Spray drift risk assessment for permethrin to non-target aquatic organisms

Organism	Exposure	Species	Endpoint reported (µg a.i./L)	Endpoint for RA[1] (µg a.i./L)	Use Scenario	Application rate [2] (g a.i./ha)	EEC (µg a.i./L)	RQ	LOC exceeded
Freshwater									
					Vegetables	3.8	0.48	**25**	Yes
					Grapes	347	43.4	**2284**	Yes
					Vegetables	3.8	0.48	**102**	Yes
					Grapes	347	43.4	**9213**	Yes
					Vegetables	3.8	0.48	0.4	No
					Grapes	347	43.4	**36**	Yes
					Vegetables	3.8	0.48	**1.6**	Yes
					Grapes	347	43.4	**144**	Yes
					Vegetables	3.8	2.53	**13**	Yes
					Grapes	347	231	**1155**	Yes
					Vegetables	3.8	2.53	**8.4**	Yes
					Grapes	347	231	**770**	Yes
	Acute				Vegetables	3.8	0.48	0.08	No
					Grapes	347	43.4	**6.9**	Yes
Marine and estuarine									
					Vegetables	3.8	0.48	**240**	Yes
					Grapes	347	43.4	**21700**	Yes
					Vegetables	3.8	0.48	**44**	Yes
					Grapes	347	43.4	**3945**	Yes
					Vegetables	3.8	0.48	0.02	No

Organism	Exposure	Species	Endpoint reported (µg a.i./L)	Endpoint for RA[1] (µg a.i./L)	Use Scenario	Application rate [2] (g a.i./ha)	EEC (µg a.i./L)	RQ	LOC exceeded
		Skeletonema costatum			Grapes	347	43.4	**1.4**	Yes
					Vegetables	3.8	0.48	0.20	No
					Grapes	347	43.4	**18**	Yes
					Vegetables	3.8	0.48	0.57	No
					Grapes	347	43.4	**52**	Yes

1- Endpoints used in the acute exposure risk assessment (RA) are derived by dividing the EC_{50}, LC_{50} from the appropriate laboratory study by a factor of two (2) for aquatic invertebrates and plants, and by a factor of ten (10) for fish and amphibians. The HC_5 is the 5th percentile of the species sensitivity distribution for the LC_{50} or NOEC at 50% confidence intervals.
2 - The assessment of potential risk from drift was assessed for the minimum single ground application for vegetables (69.12 g a.i./ha) and the maximum cumulative application rate for early airblast application for grapes (138 g a.i./ha + 4 @7d); these application rates cover the full range of application rates and application methods.
3 - The maximum amount of spray that is expected to drift 1m downwind from the application site during spraying using field sprayer (i.e., vegetables) and airblast application (i.e., grapes) method was determined based on a fine spray droplet size. 11% and 74%, respectively. The aquatic EEC for the highest cumulative application rate was revised by adjusting the sum of the applications for dissipation between applications using the DT_{50} value of 43 days ((longest of two aquatic whole system half-lives).
Bolded values indicates an exceedence of the level of concern (RQ = 1).

Table 14 Level 1 aquatic ecoscenario modelling EECs (µg a.i./L) for permethrin, overlying water layer, excluding spray drift

Rate	Depth, cm	Peak	4 day	21 day	60 day	90 day
	0.80	4.6	0.94	0.53	0.46	0.45
	0.15	24	3.7	1.3	0.79	0.67
1x69.12 g a.i./ha	0.80	0.5	0.1	0.043	0.037	0.036
	0.15	2.6	0.39	0.11	0.065	0.058

Table 15 Refined risk assessment of permethrin for aquatic organisms from predicted run-off

Organism	Exposure	Species	Endpoint reported (µg a.i./L)	Endpoint for RA[1] (µg a.i./L)	Application rate [2] (g a.i./ha)	EEC[3] (µg a.i./L)	RQ	LOC exceeded
Freshwater								
					69.12	0.50	**26**	Yes
					6x140 @7d	4.6	**242**	Yes
					69.12	0.043	**9.1**	Yes
					6x140 @7d	0.53	**113**	Yes
					69.12	0.50	0.42	No
					6x140 @7d	4.6	**3.8**	Yes
					69.12	0.043	0.14	No
					6x140 @7d	0.53	**1.8**	Yes
					69.12	2.6	**13**	Yes
					6x140 @7d	24	**120**	Yes
					69.12	0.11	0.37	No
					6x140 @7d	1.3	**4.3**	Yes
	Acute				69.12	0.50	0.08	No
					6x140 @7d	4.6	0.74	No
Marine and estuarine								
					69.12	0.50	**250**	Yes
					6x140 @7d	4.6	**2300**	Yes
					69.12	0.043	**3.9**	Yes
					6x140 @7d	0.53	**48**	Yes
					69.12	0.50	0.02	No
					6x140 @7d	4.6	0.14	No
					69.12	0.50	0.21	No

Organism	Exposure	Species	Endpoint reported (µg a.i./L)	Endpoint for RA[1] (µg a.i./L)	Application rate [2] (g a.i./ha)	EEC[3] (µg a.i./L)	RQ	LOC exceeded
					6x140 @7d	4.6	**1.9**	Yes
					69.12	0.043	0.05	No
					6x140 @7d	0.53	0.64	No

[1] Endpoints used in the acute exposure risk assessment (RA) are derived by dividing the EC_{50}, LC_{50} from the appropriate laboratory study by a factor of two (2) for aquatic invertebrates and plants, and by a factor of ten (10) for fish and amphibians.

The HC_5 is the 5th percentile of the species sensitivity distribution for the LC_{50} or NOEC at 50% confidence intervals.
[2] Application rate represents the minimum and maximum (cumulative) applications rates as indicated on labels.
[3] EEC based on a 15 cm water body depth for amphibians and a 80 cm water depth for all other aquatic organisms as determined by SWCC
Bolded values indicates an exceedence of the level of concern (RQ = 1).

Table 16 Refined risk assessment of permethrin for aquatic organisms using surface water monitoring data

Organism	Exposure	Species	Endpoint reported (µg a.i./L)	Endpoint for RA* (µg a.i./L)	EEC* (µg a.i./L)	RQ	LOC exceeded
Invertebrate	Acute	HC_5	HC_5 = 0.019	0.019		**265**	Yes
Fish	Acute	HC_5	HC_5 = 1.2	1.2		**4.2**	Yes
Amphibian	Acute	Common frog tadpoles (*Rana temporaria*)	72 h LC_{50} = 2.0	0.2		**25.2**	Yes
Algae	Acute	Green algae (*Pseudokirchneriella subcapita*)	96 h EC_{50} = 12.5	6.25		**0.81**	Yes

Bolded values indicates an exceedence of the level of concern (RQ = 1).
* The HC_5 is the 5th percentile of the species sensitivity distribution for the LC_{50} or EC_{50} at 50% confidence intervals.
** EEC based on monitoring data

Appendix VI Water monitoring data

Surface water relevant for aquatic risk assessments

For aquatic risk assessment purposes, the highest concentration of permethrin detected in water (5.04 µg/L) from a sample in New Brunswick is higher than the peak concentration predicted by modelling for water bodies 80 cm deep considering the use pattern involving six applications at 140 g a.i./ha (4.6 µg/L; Appendix IX, Table 14). Also, the highest concentration measured in water is higher than the peak EECs predicted by modelling in both the 80 cm and 15 cm waterbodies for the use pattern involving one application at 69.12 g a.i./ha (0.5 µg/L and 2.6 µg/L, respectively; Appendix IX, Table 14).

Considering only Canadian data, there were 79 detections of permethrin out of 2600 surface water samples. Due to the low detection frequency of permethrin in water and the small number of samples that were analyzed with a limit of detection low enough to detect concentrations at the level of concern for chronic risk to invertebrates, it is difficult to estimate a long term exposure concentration based on available water monitoring data.

The available Canadian water monitoring data are not robust enough to fully characterize the risks to aquatic invertebrates because 2405 out of the 2600 (93%) samples collected and analyzed for permethrin had limits of detection (LOD) which were higher than the toxicity endpoint of 0.019 µg a.i./L for aquatic invertebrates. The analytical methods were not sensitive enough to capture detections of permethrin in water that could potentially be a concern to aquatic invertebrates. Of the 195 samples with LOD sensitive enough to detect permethrin below the LOC for aquatic invertebrates, 25 (13%) exceeded the toxicity endpoint for aquatic invertebrates of 0.019 µg a.i./L (1% overall samples, or 32% of detections). Despite these deficiencies, the data still show that there are instances where concentrations were well above the toxicity endpoints. It is not possible to reliably estimate how often these occur because the toxicity endpoint is below the LOD for the majority of samples.

None of the samples from datasets for which the LOD was reported had an LOD for permethrin higher than the toxicity endpoint of 1.2 µg a.i./L for fish. A total of 53 out of the 2600 (2%) surface water samples collected in Canada had an LOD for permethrin higher than the toxicity endpoint of 1.2 µg a.i./L for amphibians. Three of the 79 detections exceeded the endpoint for fish of 1.2 µg a.i./L (equivalent to 0.1% of total number of samples, or 4% of the detections), and 9 of them exceeded the endpoint for amphibians of 0.2 µg a.i./L (0.3% of total number of samples, or 12% of the detections).

Monitoring data on transformation products of permethrin were either not available or were insufficient to estimate exposure estimates for use in an aquatic risk assessment.

Appendix VII SSD Analysis

Toxicity data analysis with Species Sensitivity Distributions (SSDs).

Background information

Toxicity data analysis may include the determination of species sensitivity distributions or SSDs in order to derive endpoints that represent the combined response of a larger "community" of species and not just the most sensitive species. The term community refers to the assemblage of species included in the SSD, also referred to as a taxonomic group, which may or may not be fully representative of the community in nature which is being modelled. The species which are used in SSDs depends on the toxicity data available and the focus of the assessment. The endpoint derived from an SSD is referred to as the hazardous concentration (HC_5), which represents the exposure level that is theoretically harmful to no more than 5% of the species and protective of 95% of the species.

An SSD is a plot of toxicity endpoints within the taxonomic assemblage of interest against a cumulative density function. The SSD is determined by fitting the dataset to an empirical distribution such as a log-normal distribution and allows the derivation of the community level threshold concentration or HC_5 and the associated confidence intervals.

The hazardous concentration to five percent of species (HC_5) is the most commonly used term with SSDs, but other terms such as the hazardous dose (HD_5) or hazardous rate (HR_5) may sometimes be used, depending on the route of exposure. For example, the term dose is relevant for birds and mammals with units of mg a.i./kg body weight, while application rate is more accurate for plants with units of g a.i./ha. However, HC_5 is commonly used as a catch-all term to describe the exposure value which is theoretically protective of 95% of all species for any route of exposure.

An SSD is constructed for various taxonomic groups where toxicity data are available and the SSD can be considered to represent the community of non-target species within the taxonomic group. If SSDs cannot be calculated the most sensitive endpoints are used with an appropriate uncertainty factor applied for risk assessment and risk mitigation.

Typical taxonomic groups used in SSDs include terrestrial organisms such as birds, mammals, invertebrates or plants and aquatic organisms such as fish, invertebrates, algae and plants. Various categories of taxonomic groups can be combined, depending on the focus of the assessment. Acute and chronic data sets are analyzed separately for SSD determinations. Acute effects are those that manifest in a short period of time, generally during exposure to a chemical stressor. Acute toxicity is considered to be a severe effect ranging from loss of equilibrium to immobility and mortality. However, less severe short term effects may also result which may be linked to more severe effects. These responses can also be considered in an acute SSD if the outcome is expected to be equivalent. If the effect levels and units are the same the measurement endpoints can be compared. This generally means that acute endpoints are those that affect survival in the short term, but in certain cases could also lead to delayed effects. Uncertainties in the effects endpoints are considered in the review.

For acute effects often the LC_{50} or EC_{50} is used as they are the most commonly reported toxicity values and represent a standard impact level on test species. However, other endpoints such as $EC_{5\text{-}10}$ may be used in order to derive lower level effects threshold values in the form of an HC_5. Still other endpoints may be used depending on the focus of the review, desired effect level or type of response one is interested in. For example, the EC_5 or EC_{25} may be used for plants or an LC_{10} may be used for fish.

To describe chronic toxicity, the no effect concentration or NOEC/NOEL is most commonly used. Chronic and sub-chronic studies have longer exposure times, generally 14 days and longer. The aim is to determine sublethal effects such as changes in reproduction, growth or other indicators of health which can result in decreased long term survival of the species. Chronic studies sometimes may report regression based EC_X values such as an EC_5/ EC_{10}. The EC_{10} derived from chronic single species exposure studies measuring sublethal effects is often considered as equivalent to a NOEC which is derived from hypothesis testing, and may be considered relevant / appropriate to the assessment. Single species chronic studies yield NOEC values based on Analysis of Variance. The NOEC concentrations may still have a considerable biological adverse effect, therefore scientific judgement is used to interpret the results.

The intent of ecological modelling is to derive an environmental concentration for chemicals that are below all or close to all species' toxicity values, for both acute and chronic effects. Due to practical limitations in modelling, however, traditionally a 95% protection level has been used as a reasonable approximation of an acceptable level of protection for each taxonomic group. The HC_5 is the concentration which is assumed to be protective for 95% of species in a taxonomic group or assemblage (for example freshwater fish) as related to the assessment endpoint and ecological protection goal. The term *protective* means that 95% of species are not expected to be exposed to concentrations above the species specific threshold toxicity value, such as the LC_{50}, EC_X or NOEC. However, 5% of all species are expected to be impacted according to the data that was used in the SSD. In other words, on average, five percent of all species within a taxon could be exposed to concentrations of a pesticide which would produce fifty percent mortality in those species if the LC_{50} values were used to derive the SSD.

In practice and under field conditions, the percent of species affected or the impact level within species may vary as the HC_5 has inherent variability, leading to the possibility that either more or less than five percent of the species would experience mortality for example. Therefore, it is important to note the 90% confidence intervals of the fraction of species affected (FA) in addition to that of the HC_5 value.

SSDs use all the available toxicity information, thereby reducing but not eliminating the uncertainty in risk estimates which is inherent with single species tests. SSDs provide a scientifically more robust and ecologically relevant endpoint versus single toxicity values, in the form of an HC_5. The SSD represents a sub-set of the real potential range of sensitivity in the non-target community and is therefore better suited to estimate risk and inform mitigation measures.

The software program ETX 2.1 is used to generate SSDs. The median HC_5 and confidence values are reported for SSDs, however, for risk assessment and mitigation purposes, an uncertainty factor or the lower confidence level may be used. The variability in the data sets is indicated not only by the 90% upper and lower bound HC_5 estimates but also the confidence limit of the fraction of species affected (FA), which indicates the theoretical minimum and maximum percent of species that could be affected when the population is exposed to the HC_5 concentration.

Where multiple data points are available for one species, a geometric mean value is used to represent the species' sensitivity. The treatment of toxicity data is such as to allow consistent quantitative estimates for various pesticides and ensures that certain criteria are met including the use of equivalent exposure units, ecological relevance and comparability of measurement endpoints, types of test chemicals, duration of exposure and other parameters.

Results of SSD analysis for permethrin insecticide: Distributions were determined for the following taxonomic groups (results are reported in summary Table 1):

- Freshwater invertebrates
- Freshwater fish
- Marine invertebrates
- Marine fish

The confidence intervals (CI) on the HC_5 and the fraction of species affected (FA) are relatively large for all four taxonomic groups, indicating high variability in the data sets. This indicates that a potentially high fraction of species could be affected above the 5% level. For example, as a worst case scenario, up to 12.9% of all freshwater invertebrates could be affected at an EC_{50} level of effect if exposed to 0.019 µg a.i./L of permethrin, while up to 18.9% of marine invertebrate species could be affected from exposure to 0.002 µg a.i./L. Both freshwater and marine fish have sensitivities of 2-3 orders of magnitude lower than aquatic invertebrates; however, the data shows wide variations with the fraction of species affected reaching up to 11.7-20% as shown in Table 1 below.

Table 1 Summary of Species Sensitivity Distribution (SSDs) toxicity data analysis for permethrin insecticide: The HC_5[1] values (or the most sensitive endpoints*) are listed by taxonomic group.

Exposure	Freshwater invertebrates (µg a.i./L)	Freshwater fish (µg a.i./L)	Marine invertebrates (µg a.i./L)	Marine fish (µg a.i./L)
	HC_5: 0.019 (EC_{50}) Species count: 25	HC_5: 1.2 (LC_{50}) Species count: 30	HC_5: 0.002 (EC_{50}) Species count: 11	HC_5: 2.4 (LC_{50}) Species count: 10
	CI: 0.0043-0.057 FA: 1.5-12.9%	CI: 0.66-1.9 FA: 1.7-11.7%	CI: 0.00003-0.0237 FA: 0.7 – 18.9%	CI: 0.77-4.4 FA: 0.6-20.0%
Chronic	NOEC: 0.0047 (21d)	NA	NA	NA

(CI) = 90% lower and upper confidence level of HC_5; (FA) = fraction of species affected (90% CI); NA: data are not shown; (EC_{50}/LC_{50}): HC_5 is based on this endpoint; *Where SSDs could not be determined, the most sensitive species endpoint is reported; [1]The Hazardous concentration to 5% of species is theoretically protective of 95% of all species at the effect level used in the analysis.

Table 2.1 Marine fish species used in SSDs

Marine fish	
Species name	**Toxicity value (µg a.i./L)**
Sheepshead minnow	43.3
Topsmelt	25.3
Adult mummichog	22.9
Leon Springs pupfish	21.0
Coho salmon	17.0
Inland silversides	10.4
Juvenile red drum	8.5
Stripped mullet	5.5
Atlantic salmon	4.2
Atlantic silverside	2.2

Table 2.2 Freshwater fish species used in SSDs

Freshwater fish	
Species name	**Toxicity value (µg a.i./L)**
Redbelly tilapia *Tilapia zillii*	49.0
Guppy	46.8
Tilapia mossambica	44.0
Common carp	35.0
Nile tilapia *Oreochromis niloticus*	27.0
Elephant fish	26.0
Bonytail chub	25.0
Colorado pikeminnow	24.4
Western mosquito fish	23.3
Japanese medaka fish	17.8
Zebra fish	15.6
Rainbow trout	13.3
Fathead minnow	11.0
Gila topminnow	10.0
Largemouth bass	8.5
Bluegill sunfish	6.8
Razorback sucker	6.0
Bleak	5.6
Desert pupfish	5.0
Cape Fear shiner	4.2
Brook trout	3.5
Channel catfish	3.5
Fountain darter	3.3
Indian major carp *Labeo rohita*	3.1
Brook trout	2.9
Greenthroat darter	2.7
Apache trout	1.7
Spotfin chub	1.7
Lahontan cut-throat trout	1.6
Greenback cut-throat trout	1.0

Table 2.3 Freshwater invertebrate species used in SSDs

Freshwater invertebrates	
Species name	**Toxicity value (µg a.i./L)**
Crayfish *Procambarus blandingii*	210.00
Glochidia freshwater mussel *Villosa delumbis*	200.00
Chironomus thummi	16.60
Mayfly *larvae Baetis hodani*	12.00
Chironomus tentans	10.45
Mosquito larvae *Aedes triseriatus*	6.62
Mosquito larvae *Aedes atropalpus*	6.17
Mosquito larvae *Aedes hendersoni*	3.50
Chironomus riparius	2.89
Mosquito larvae *Aedes albopictus*	0.95
Red Swamp Crayfish *Procambarus clarkii*	0.80
Daphnia magna	0.81
Lesser water boatman (adults) *Corixa punctata Illiger)*	0.70
Ceriodaphnia dubia	0.63
Chironomus plumosus	0.56
Yellow fever mosquito *Aedes aegypti*	0.45
Caddisfly larvae *Brachycentrus americanus*	0.40
Amphipod *Gammarus pulex*	0.24
Scud *Gammarus pseudolimnaeus*	0.17
Stonefly larvae *Pteronarcys dorsata*	0.15
Blackfly Simulium spp.	0.14
Hexagenia bilineata	0.10
Chironomus dilutes	0.06
Mayfly larvae *Cloen dipterum* (L); early instar	0.03
Hyalella azteca	0.03

Table 2.4 Marine invertebrate species used in SSDs

Marine invertebrates	
Species name	**Toxicity value (µg a.i./L)**
Crassostrea gigas	2612.5
Crassostrea virginica	602.0
Uca pugilator	3.20
Homerus americanus	0.73
Penaeus aztecus	0.34
Nitocra spinipes	0.30
Penaeus duorarum	0.29
Palaemonetes pugio	0.28
Crangon septemspinosa	0.13
Americamysis bahia	0.06
Menippe mercaria	0.018

Appendix VIII Toxic Substances Management Policy

Table 1 Toxic Substances Management Policy Considerations - Comparison to TSMP Track 1 Criteria

TSMP Track 1 Criteria	TSMP Track 1 Criterion value		Permethrin Are criteria met?
CEPA toxic or CEPA toxic equivalent[1]	Yes		Yes
Predominantly anthropogenic[2]	Yes		Yes
	Soil	Half-life ≥ 182 days	No: 8 – 113 days
	Water	Half-life ≥ 182 days	not applicable, permethrin is insoluble
	Whole system (Water + Sediment)	Half-life ≥ 365 days	No: 38 – 43 days
	Air	Half-life ≥ 2 days or evidence of long range transport	No: AOPWIN calculated half-life in air is 0.70 days.
	Log Kow ≥ 5		Yes: 6.1
	BCF ≥ 5000		No: <1100 (fish)
	BAF ≥ 5000		No: <2714 (fish)
Is the chemical a TSMP Track 1 substance (all four criteria must be met)?			**No, does not meet all TSMP Track 1 criteria.**

[1]All pesticides will be considered CEPA-toxic or CEPA toxic equivalent for the purpose of initially assessing a pesticide against the TSMP criteria. Assessment of the CEPA toxicity criteria may be refined if required (i.e., all other TSMP criteria are met).
[2]The policy considers a substance "predominantly anthropogenic" if, based on expert judgment, its concentration in the environment medium is largely due to human activity, rather than to natural sources or releases.
[3] If the pesticide and/or the transformation product(s) meet one persistence criterion identified for one media (soil, water, sediment or air) than the criterion for persistence is considered to be met.
[4]The log K_{OW} and/or BCF and/or BAF are preferred over log K_{OW}.

Appendix IX Label Amendments for Products Containing Permethrin

The label amendments presented below do not include all label requirements for individual end-use products, such as first aid statements, disposal statements, precautionary statements and supplementary protective equipment. Additional information on labels of currently registered products should not be removed unless it contradicts the label statements given below.

I. TECHNICAL GRADE ACTIVE INGREDIENTS AND COMMERCIAL CLASS PRODUCTS

The following is proposed to be added the labels of the technical grade active ingredients and all end-use products under the section entitled **Toxicological Information**

"Skin exposure may cause transient sensations (tingling, burning, itching, numbness). Treat symptomatically."

II. TECHNICAL GRADE ACTIVE INGREDIENTS

1. The following statements are proposed to be added to the **Environmental Hazards/Precautions** section:

"TOXIC to aquatic organisms."

"DO NOT discharge effluent containing this product into sewer systems, lakes, streams, ponds, estuaries, oceans or other waters."

2. The following statements are proposed to be added to the **Disposal** section:

"Canadian manufacturers should dispose of unwanted active ingredients and containers in accordance with municipal or provincial regulations. For additional details and clean up of spills, contact the manufacturer or the provincial regulatory agency."

III. COMMERCIAL CLASS PRODUCTS

1. The following label statements are proposed to be added on labels for agricultural food/feed crop uses:

"A plant back interval of 60 days is required for all non-registered agricultural food/feed crops."

"For use on tomato, DO NOT apply more than five applications per year."

2. The following label updates are required for certain products registered for uses on livestock and livestock housing:

Poultry:

- Liquid application on poultry for control of northern fowl mites at a rate of 0.019 g a.i./animal/application with a maximum of 2 applications/year, a minimum re-treatment interval (RTI) of 14 days and a minimum pre-slaughter interval (PSI) of 7 days, using knapsack and handgun; and
- Poultry housing application at a rate of below 0.05 a.i./m^2 (for example, 0.0398 and 0.048 g a.i./m^2) with a maximum of 12 applications/year, a minimum RTI of 14 days and a minimum PSI of 1 day, or at a rate of above 0.05 g a.i./m^2 but less or equal to 0.1 g a.i./m^2 (for example, 0.096 and 0.1 g a.i./m^2) with a maximum of 12 applications/year, a minimum RTI of 14 days and a minimum PSI of 7 days.

Cattle:

- Ear tag for control of face flies and horn flies with a maximum of two ear tags/animal/year, each ear tag containing a maximum of 0.95 g permethrin, and a minimum PSI of 1 day;
- Self-oiler for control of black flies, face flies, gnats, horn flies and mosquitoes at a maximum rate of 0.125 g a.i./animal/application and a minimum PSI of 1 day;
- Pressurized product for control of face flies, horn flies, gnats and mosquitoes at a rate of 0.045 g a.i./animal/application and a minimum PSI of 1 day;
- Pour-on, cloth for control of biting lice, sucking lice, horn flies, rocky mountain wood tick at a rate of 1.3 g a.i./animal/application with a maximum of 2 applications/year, a minimum RTI of 14 days and a minimum PSI of 1 day, as well as a the existing statement of "For Dairy Cattle DO NOT use this product in combination with any other permethrin treatment.";
- Liquid application on beef cattle and non-lactating dairy cattle for control of black flies, mosquitoes, face flies, horn flies and lice at a rate of 0.96 g a.i./animal/application with a maximum of 2 applications/year, a minimum RTI of 8 days and a minimum PSI of 7 days, using knapsack, handgun and low pressure sprayer;
- Liquid application on beef cattle only for control of rocky mountain wood tick at a rate of 1.5 g a.i./animal/application with a maximum of 2 applications/year, a minimum RTI of 14 days and a minimum PSI of 7 days, using high pressure sprayer; and
- Cattle housing application at a rate of below 0.05 a.i./m^2 (for example, 0.0398 and 0.048 g a.i./m^2) with a maximum of 12 applications/year, a minimum RTI of 14 days and a minimum PSI of 1 day, or at a rate of above 0.05 g a.i./m^2 but less or equal to 0.1 g a.i./m^2 (for example, 0.096 and 0.1 g a.i./m^2) with a maximum of 12 applications/year, a minimum RTI of 14 days and a minimum PSI of 7 days.

Sheep:

- Pressurized product for control of sheep ked at a rate of 0.045 g a.i./animal/application with a minimum PSI of 1 day;
- Liquid application for control of sheep ked at a rate of 0.144 g a.i./animal/application with a maximum of 1 application/year and a minimum PSI of 1 day using knapsack and handgun; and
- Sheep housing application at a rate of below 0.05 a.i./m^2 (for example, 0.0398 and 0.048 g a.i./m^2) with a maximum of 12 applications/year, a minimum RTI of 14 days and a minimum PSI of 1 day, or at a rate of above 0.05 g a.i./m^2 but less or equal to 0.1 g a.i./m^2 (for example, 0.096 and 0.1 g a.i./m^2) with a maximum of 12 applications/year, a minimum RTI of 14 days and a minimum PSI of 7 days.

Horse:

- Pressurized product for control of black flies, face flies, gnats, horn flies, horse flies, house flies and mosquitoes at a rate of 0.045 g a.i./animal/application with a minimum PSI of 1 day; and
- Horse housing application at a rate of below 0.05 a.i./m^2 (for example, 0.0398 and 0.048 g a.i./m^2) with a maximum of 12 applications/year, a minimum RTI of 14 days and a minimum PSI of 1 day, or at a rate of above 0.05 g a.i./m^2 but less or equal to 0.1 g a.i./m^2 (for example, 0.096 and 0.1 g a.i./m^2) with a maximum of 12 applications/year, a minimum RTI of 14 days and a minimum PSI of 7 days.

Swine housing:

- Swine housing application at a rate of below 0.05 a.i./m^2 (for example, 0.0398 and 0.048 g a.i./m^2) with a maximum of 12 applications/year, a minimum RTI of 14 days and a minimum PSI of 1 day, or at a rate of above 0.05 g a.i./m^2 but less or equal to 0.1 g a.i./m^2 (for example, 0.096 and 0.1 g a.i./m^2) with a maximum of 12 applications/year, a minimum RTI of 14 days and a minimum PSI of 7 days.

3. For treatment of wood using an enclosed linear system, the following statement should be added to the pest listed under **Directions For Use**.

"Ambrosia and wood boring beetles in sawn lumber for export to Australia."

4. In order to promote best practices, and to minimize human exposure from spray drift or from spray residues resulting from drift due to the agricultural use of permethrin, the following label statements are proposed for commercial-class labels:

"Apply only when the potential for drift to areas of human habitation or areas of human activity such as houses, cottages, schools, and recreational areas in minimal. Take into consideration wind speed, wind direction, temperature inversions, application equipment, and sprayer settings."

"Do not apply this product using fogging equipment (hand-held or automated), or using hand-held mist blowers/airblast equipment."

"Not for use in mushroom houses."

5. The following should be added to the commercial-class labels for residential areas, when necessary:

"DO NOT apply indoors as a broadcast application. ONLY band, spot or crack and crevice applications are permitted. Band application is defined as an application in a band or strip (less than 0.3 m wide) around the perimeter of the room (baseboards or ceiling) or over a small area (<2 ft^2/0.2 m^2). Crack and crevice applications are defined as an application with the use of a pin stream nozzle, into cracks and crevices in which pests hide or through which they may enter a building. Such openings commonly occur at expansion joints, between different elements of construction, between equipment and floors, and junction or switch boxes."

"Residential areas are defined as any use site where the general public, including children, could be exposed during or after application. For structural uses, in residential sites, this includes homes, schools, restaurants, public buildings or any other areas where the general public including children may potentially be exposed. Non-residential areas include, but are not limited to: industrial/commercial indoor sites (for example, laboratories, warehouses, food granaries); modes of transport in areas where passengers are not present (for example, buses, railcars, trailers); and animal housing (for example, livestock housing and poultry, pet kennels)."

6. The following statements should be added to all commercial-class labels for products used in residential areas (except products for aircraft disinsection):

"DO NOT allow people or pets to enter treated areas until sprays have dried."

"DO NOT apply to overhead areas or in confined spaces without appropriate/adequate respiratory and eye protection."

"Ventilate treated areas during application either by opening windows and doors or through use of air exchange/ventilation systems confirmed to be operational. Use fans where required to aid in the circulation of air."

7. The following statements should be added to commercial-class space spray product labels for residential areas (except products for aircraft disinsection):

"DO NOT allow people or pets to enter treated areas until 15 minutes after application."

8. Statements on all commercial-class agricultural permethrin labels must be amended (or added) to include the following directions:

"Wear long pants, long-sleeved shirts, and chemical-resistant gloves during mixing, loading, application, clean-up, and repair activities."

9. For all mechanically pressurized handgun applications in non-agricultural areas (e.g. residential, commercial, and industrial), the following label statement should be added to commercial-class labels:

"For mechanically pressurized handgun applications, wear cotton coveralls over long-sleeved shirt, long pants and chemical-resistant gloves."

10. For truckmounted mist blower or airblast applications for mosquito abatement, the following label statement should be added to commercial-class labels:

"For truck mounted mist blower or airblast applications, wear a long-sleeved shirt, long pants, chemical-resistant gloves, and a chemical-resistant hat that covers the neck (e.g Sou'Wester)."

11. For wood treatment in an enclosed linear system, the following statements should be added:

"Wear chemical-resistant coveralls over long-sleeved shirt and long pants, chemical-resistant gloves, goggles or face shield, socks, and chemical-resistant footwear when handling the concentrate or during mixing/loading, application, clean-up, maintenance and repair activities."

"Use a NIOSH-respirator if the area is not well ventilated and during clean-up, maintenance and repair activities ."

"When piling freshly-treated lumber or if there is a potential for getting wet by the treating solution or by handling freshly-treated lumber, wear chemical-resistant coveralls over long-sleeved shirt and long pants, chemical-resistant gloves, socks and chemical-resistant footwear."

"When working in the dip or spray area, wear a long-sleeved shirt, long pants, chemical-resistant gloves, socks, and boots. Wear goggles or face shield if there is a possibility of splashing."

"Once dry, the treated wood can be handled with cotton or leather gloves."

"Wash hands and face before eating, drinking, smoking and using the toilet. Change clothes daily. Wash contaminated clothing separately from household laundry. Not for use or storage in or around the home. Clean contaminated equipment thoroughly prior to making welding repairs."

12. For wood treatment in an enclosed linear system, references to aprons should be removed due to potential physical hazard concerns (that is, aprons getting caught in machinery).

13. Consult the following table regarding REIs. Where deemed necessary, REIs are subdivided according to re-entry activities. These restricted entry intervals must be added to the appropriate commercial-class labels as listed below:

Proposed Restricted Entry Intervals

Crop	Activity	REI (days) [a]
apple, nectarine, peach, pear, plum, asparagus, barley, canola, cereals, flax, oats, peanuts, peas, rape, rye, snap bean, sugar beet, wheat, lentils, beet, carrot, onion, potato, turnip, radish, wasabi, ginseng, horseradish, low bush blueberry, lettuce, pak choi, tomato, pepper, tobacco, commercial woodland, broccoli, Brussels sprouts, cabbage, cauliflower, Chinese broccoli, Chinese cabbage, cole crops, conifer/tobacco seedlings, ornamentals, greenhouse tomato, greenhouse cucumber, fence rows, sunflowers	All activities	0.5
	all other activities	0.5
	tying/training, leaf pulling	2
	girdling, turning	15
	all other activities	0.5
	tying/training, hand harvesting, leaf pulling	2
	girdling, turning	15
	all other activities	0.5
	hand detasseling, hand harvest	8

[a] Day at which the dermal exposure results in an MOE ≥ 300.

IV. DOMESTIC CLASS PRODUCTS (except treated clothing):

1. The following statement should be added to the domestic-class labels, when necessary:

"DO NOT apply indoors as a broadcast application. Apply ONLY into the cracks and crevices where pests hide or through which they may enter a building. This is includes around the outside edges of a room (baseboards), doorways and/or windows."

2. The following statements should be added to all domestic-class labels:

"DO NOT apply by hand-held mist blower/sprayer or fogger."

"DO NOT apply to overhead areas or in confined spaces (attics, crawlspaces etc.)."

"Ventilate treated areas either by opening windows and doors or through use of air exchange/ventilation systems. Use fans where required to aid in the circulation of air."

"DO NOT allow people or pets to enter treated areas until sprays have dried."

3. The following statement should be added to domestic-class space spray product labels:

"DO NOT allow people or pets to enter treated areas until 15 minutes after application."

V. ALL END-USE PRODUCTS (DOMESTIC AND COMMMERCIAL)

1. The following statement is proposed to be added to all **lawn and turf** labels:

"DO NOT apply more than 0.123 g a.i./m^2."

2. The following statements are proposed to be added to the **Environmental Precautions** section of all end-use product labels:

"TOXIC to aquatic organisms. Observe buffer zones specified under DIRECTIONS FOR USE."

"Toxic to birds."

"TOXIC to bees. Bees may be exposed through direct spray, spray drift, and residues on leaves, pollen and nectar in flowering crops and weeds. Minimize spray drift to reduce harmful effects on bees in habitats close to the application site. Avoid applications when bees are foraging in the treatment area in ground cover containing blooming weeds. To further minimize exposure to pollinators, refer to the complete guidance "Protecting Pollinators during Pesticide Spraying – Best Management Practices" on the Health Canada website (www.healthcanada.gc.ca/pollinators). Follow crop specific directions for application timing."

For crops that are highly attractive to pollinators (apples, pears, nectarines, peaches, plums, canola, sunflowers) or when using managed bees for pollination services:

> "Do not apply during the crop blooming period."

For all other crops:

> "Avoid application during the crop blooming period. If applications must be made during the crop blooming period, restrict applications to evening when most bees are not foraging."

"Toxic to certain beneficial insects. Minimize spray drift to reduce harmful effects on beneficial insects in habitats next to the application site such as hedgerows and woodland. Permethrin may impact predatory and parasitic arthropod species used in IPM programs within the treatment area. Unsprayed refugia for beneficial species of at least 1 metre from treatment area will help maintain beneficial arthropod populations."

"To reduce runoff from treated areas into aquatic habitats avoid application to areas with a moderate to steep slope, compacted soil, or clay."

"Avoid application of this product when heavy rain is forecast."

"Construct and maintain a minimum 10 meter wide vegetative filter strip of grass or other permanent vegetation between the field edge and any aquatic habitat down gradient from the area of application. These aquatic habitats include, but are not limited to, lakes, reservoirs, rivers, permanent streams, marshes or natural ponds, estuaries and commercial fish farm ponds."

"Only apply products containing permethrin onto fields where a maintained vegetative filter strip of at least 10 meters exists between the field and aquatic habitat down gradient of area of application."

"To use this product you must maintain a vegetative filter strip of at least 10 metres designed to remove sediment. The design of the filter strip should follow existing federal or provincial guidance such as that found at: http://www.agr.gc.ca/eng/science-and-innovation/agricultural-practices/agroforestry/shelterbelt-planning-and-establishment/design/riparian-buffers/?id=1344888191892 and http://www.agr.gc.ca/fra/science-et-innovation/pratiques-agricoles/agroforesterie/planification-et-etablissement-des-brise-vent/conception/bandes-riveraines/?id=1344888191892"

3. The following statement is proposed to be added for all greenhouse uses:

   "Greenhouse use: Toxic to bees and other beneficial insects. May harm bees and other beneficial insects, including those used in greenhouse production. Do not apply when bees or other beneficial insects are foraging in the treatment area."

4. The following statements are proposed to be added to the **Directions for Use** section on all product labels:

   "To protect pollinators, follow the instructions regarding bees in the Environmental Precautions section."

   For apples, pears, nectarines, peaches, plums, canola, sunflowers include:
   "Toxic to bees. DO NOT apply during the crop blooming period."

   For all other crops on label (excluding barley, oats, rye, wheat, triticale):
   "Toxic to bees. Avoid application during the crop blooming period. If applications must be made during the crop blooming period, restrict applications to evening when most bees are not foraging. When using managed bees for pollination services, DO NOT apply during the crop blooming period."

   "As this product is not registered for the control of pests in aquatic systems, DO NOT use to control aquatic pests."

   "DO NOT contaminate irrigation or drinking water supplies or aquatic habitats by cleaning of equipment or disposal of wastes."

   "Field sprayer application: **DO NOT** apply during periods of dead calm. Avoid application of this product when winds are gusty. **DO NOT** apply when wind speed is greater than 8 km/h at the site of application. **DO NOT** apply with spray droplets smaller than the American Society of Agricultural Engineers (ASAE S572.1) medium classification. Air-induction nozzles must be used for the ground application of this product. Boom height must be 60 cm or less above the crop or ground.

Airblast application: **DO NOT** apply during periods of dead calm. Avoid application of this product when winds are gusty. **DO NOT** direct spray above plants to be treated. Turn off outward pointing nozzles at row ends and outer rows. **DO NOT** apply when wind speed is greater than 16 km/h at the application site as measured outside of the treatment area on the upwind side.

Aerial application: **DO NOT** apply during periods of dead calm. Avoid application of this product when winds are gusty. **DO NOT** apply when wind speed is greater than 10 km/h at flying height at the site of application. **DO NOT** apply with spray droplets smaller than the American Society of Agricultural Engineers (ASAE S572.1) medium-coarse classification. **DO NOT** apply under weather conditions of less than 50% relative humidity and temperatures greater than 20°C. To reduce drift caused by turbulent wingtip vortices, the nozzle distribution along the spray boom length **MUST NOT** exceed 65% of the wing- or rotorspan.

Buffer zones:

Use of the following spray methods or equipment **DO NOT** require a buffer zone: hand-held or backpack sprayer and spot treatment.

The buffer zones specified in the table below are required between the point of direct application and the closest downwind edge of sensitive freshwater habitats (such as lakes, rivers, sloughs, ponds, prairie potholes, creeks, marshes, streams, reservoirs and wetlands) and estuarine/marine habitats.

Method of application	Crop		Buffer Zones (metres) Required for the Protection of:			
			Freshwater Habitat of Depths:		Estuarine/Marine Habitats of Depths:	
			Less than 1 m	Greater than 1 m	Less than 1 m	Greater than 1 m
	Sweet corn		35	15	75	35
	Ginseng, carrots		20	10	45	20
	Broccoli, Brussel sprouts, cabbage, cauliflower, peppers, potatoes		35	15	75	35
	Canola, asparagus, barley, beets, field corn, flax, lettuce, oats, onions, peas, rye, sunflower, triticale, wheat, lentils		10	5	25	10
	Turnip, snap beans		15	5	30	15
	Chinese broccoli, wasabi, horseradish, pakchoï, peanuts, radish, tobacco		20	10	40	20
	Blueberries		5	3	15	5
	Tomato		45	20	90	40
		Early	75	65	80	70
		Late	60	55	70	60

Method of application	Crop		Buffer Zones (metres) Required for the Protection of:			
			Freshwater Habitat of Depths:		Estuarine/Marine Habitats of Depths:	
			Less than 1 m	Greater than 1 m	Less than 1 m	Greater than 1 m
	Nectarines, peach	Early	80	70	85	80
		Late	70	60	75	65
		Early	80	70	90	80
		Late	70	60	75	70
		Early	80	70	90	80
		Late	70	60	80	70
		Early	60	55	70	60
		Late	50	45	60	50
		Early	80	70	90	80
		Late	70	60	80	70
	PCP #14882					
		Fixed-wing	800	800	800	800
		Rotary-wing	800	700	800	800
		Fixed-wing	800	800	800	800
		Rotary-wing	800	550	800	800
		Fixed-wing	800	800	800	800
		Rotary-wing	800	700	800	800
	PCP #16688					
		Fixed-wing	800	800	800	800
		Rotary-wing	800	575	800	800
		Fixed-wing	800	575	800	800
		Rotary-wing	650	375	800	625
		Fixed-wing	800	750	800	800
		Rotary-wing	800	500	800	800
	PCP #28877					
		Fixed-wing	800	800	800	800
		Rotary-wing	800	575	800	800

Method of application	Crop		Buffer Zones (metres) Required for the Protection of:			
			Freshwater Habitat of Depths:		Estuarine/Marine Habitats of Depths:	
			Less than 1 m	Greater than 1 m	Less than 1 m	Greater than 1 m
	Broccoli, cauliflower, cabbage, asparagus, barley, beets, carrots, field corn, flax, lettuce, oats, onions, peas, potato, rye, sunflower, triticale, wheat, Brussel sprouts, peppers, canola, lentils	Fixed-wing	800	600	800	800
		Rotary-wing	650	375	800	625
		Fixed-wing	800	800	800	800
		Rotary-wing	800	475	800	800

For tank mixes, consult the labels of the tank-mix partners and observe the largest (most restrictive) buffer zone of the products involved in the tank mixture and apply using the coarsest spray (ASAE) category indicated on the labels for those tank mix partners.

The buffer zones for airblast application of this product can be modified based on weather conditions and spray equipment configuration by accessing the Buffer Zone Calculator on the Pest Management Regulatory Agency web site. Buffer zones for field sprayer or aerial application CANNOT be modified using the Buffer Zone Calculator."

5. The following statements are proposed to be added for greenhouse use:

"Toxic to bees and other beneficial insects. May harm bees and other beneficial insects including those used in greenhouse production. Do not apply when bees or other beneficial insects are foraging in the treatment area."

"DO NOT allow effluent or runoff from greenhouses containing this product to enter lakes, streams, ponds or other waters."

References

A. Studies Considered in the Chemistry Assessment

List of Studies/Information Submitted by Registrant

1491644	2004, Syngenta Crop Protection Canada Inc. / Confidential Cross Reference 2, DACO: 2.11.2
1491645	2004, Syngenta Crop Protection Canada Inc. / Confidential Cross Reference 3, DACO: 2.11.3
1073300	Permethrin: Physical Properties . 9 pages. [Complete Study Under Tab 2.16], DACO: 2.16 CBI
1073303	Permethrin Product Identity and Disclosure of Ingredients, Description of Starting Materials and Manufacturing Process, Discussion on the Formation of Impurities, Physical and Chemical Properties. [Complete Study Under Tab 2.16], DACO: 2.16 CBI
2459655	2010, Permethrin Technical (XD): Analysis and Certification of Product Ingredients, DACO: 2.13.3 CBI
1266955	1999, Permethrin: Physical/Chemical Properties, DACO: 2.14.1,2.14.10,2.14.11, 2.14.12,2.14.13,2.14.14,2.14.2,2.14.3,2.14.4,2.14.5,2.14.6,2.14.7,2.14.9 CBI
1266951	Manufacturing Summary, DACO: 2.11.1 CBI
1266954	1999, Permethrin: Product Identity, Composition And Analysis, DACO: 2.11.2,2.11.3,2.11.4 CBI
2410250	2012, PRELIMINARY ANALYSES OF FIVE REPRESENTATIVE PRODUCTION BATCHES OF PERMETHRIN TECHNICAL GRADE ACTIVE INGREDIENT (TGAI) TO DETERMINE % PERMETHRIN AND TO QUANTIFY ITS ASSOCIATED IMPURITIES, DACO: 2.13.3
2410252	2012, PRELIMINARY ANALYSES OF FIVE REPRESENTATIVE PRODUCTION BATCHES OF PERMETHRIN TECHNICAL GRADE ACTIVE INGREDIENT (TGAI) TO DETERMINE % PERMETHRIN AND TO QUANTIFY ITS ASSOCIATED IMPURITIES - confidential attachment, DACO: 2.13.3 CBI
1357319	2004, Product Identity and Composition of Pramex B Technical Insecticide, DACO: 2.11.1,2.11.2,2.11.3,2.11.4,2.12.1,2.12.2,2.13.4,2.4,2.5,2.6,2.7 CBI
2634340	2011, Characterization of Five Lots of Technical Grade Permethrin, DACO: 2.13.1 CBI
2634345	2016, Manufacturing Dates, DACO: 2.13.1,2.13.3 CBI

B. Studies Considered in the Toxicological Assessment

List of Studies/Information Submitted by Registrant

PMRA Document Number	Reference
2127251	1977, Permethrin: Tissue retention in the Rat: Report No. CTL/P/352, DACO 4.5.9
2127252	1990, Permethrin: Summary of MRID 41560203 the Metabolism of [14C]-Permethrin in the Rat, DACO 4.5.9
2127253	1976, PP557: Absorption and Excretion in the Rat, DACO 4.5.9
2127254	1989, Permethrin: the Metabolism of [14C]-Permethrin in the Rat, DACO 4.5.9
2127256	1990, Phase 3 Summary of MRID 54719 PP557: Absorption and Excretion in the Rat: Report No. CTL/P/228, DACO 4.5.9
2127258	1990, Phase 3 Summary of MRID 00089006 and Related MRIDs 00054720, Permethrin: Tissue Retention in the Rat: Report No. CTL/P/352, DACO 4.5.9
1403351	1976, Permethrin Metabolism in Rats and Cows and in Bean and Cotton Plants, DACO 4.5.9
2127255	1990, Phase 3 Summary of MRID 57092, 65093 and 110642, Permethrin Metabolism in Rats, DACO 4.5.9
2127289	1977, Permethrin: Tissue Retention in the Dog, CTL/P/353, DACO 6.4
2127290	1977, Absorption, Distribution and Excretion in the Dog, CTL/P/285, DACO 6.4
2035764	1983, Dermal Penetration and Distribution of 14C-Labeled Permethrin Isomers , DACO 4.5.9
1237289	1989, Permethrin: Acute oral toxicity to the rat, CTL/P/2453, DACO 4.2.1
2045473	1988, Final Phase - The Effects of Laundering on the Permethrin Content of Impregnated Military Fabrics, DACO 5.9
1237261	1989, Permethrin: 4-hour Acute Inhalation Toxicity Study in the Rat, CTL/P/2492, DACO 4.2.3
1237262	1989, Permethrin: Eye Irritation to the Rabbit, CTL/P/2455, DACO 4.2.4
1237263	1989, Permethrin: Skin Irritation to the Rabbit, CTL/P/2452, DACO 4.2.5
1237264 and 2127226	1989, Permethrin: Skin Sensitization Study, CTL/P/2456, DACO 4.2.6
1403361	1976, Toxicity Studies on the Insecticide WL 43479: A Five Week Feeding Study in Rats, DACO 4.3.3
1403362	1976, A Three Month Oral Toxicity Study of FMC 33297 in Rats and Addendum, DACO 4.3.1
2127227	1975, Six-month Subacute Oral Toxicity of NRDC 143 in Sprague Dawley Rats, DACO 4.3.1
1403363	1976, A Three Month Oral Toxicity Study of FMC 33297 in Beagle Dogs, DACO 4.3.2

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C. Information Considered in the Dietary Assessment

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2127276	The Metabolite Profiles In Tissues, Milk And Urine Of Cows After Dermal Application Of (Carbon 14) Permethrin
2127277	Permethrin: Absorption In Chickens After Dermal And Oral Treatments
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2127381	Permethrin Residues On Cabbage
2127382	Permethrin Metabolite Residues In Cabbage
2127383	Permethrin Residues In Brussels Sprouts
2127384	Permethrin Residues On Cauliflower
2127385	Permethrin Residues On Broccoli
2127386	Permethrin Residues On Pears
2127387	Permethrin Residues On Grapes
2127388	Permethrin Residues In Eggplant, Cumberland County, New Jersey - 1978
2127389	Permethrin Metabolite Residues On Sweet Corn
2127390	Permethrin Residues In Fresh And Canned Pears
2127391	Permethrin Metabolite Residues On Broccoli
2127392	Permethrin Metabolite Residues On Cauliflower
2127393	Permethrin Metabolite Residues On Brussels Sprouts
2127394	Permethrin Residues On Tomatoes
2127395	Permethrin Residues On Sweet Corn
2127396	Permethrin Residues On Apples
2127397	Permethrin Metabolite Residues On Tomatoes
2127398	Ambush: Permethrin Metabolite Residues On Soybeans
2127399	Permethrin Residues On Potatoes
2127400	Permethrin Metabolite Residues On Apples
2127401	Ambush: Permethrin Residues From Aerial Applications To Soybeans

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2127402	Ambush: Permethrin Metabolite Residues On Potatoes
2127403	AMBUSH: Permethrin Residues On Alfalfa
2127404	Permethrin Metabolite Residues On Alfalfa
2127406	Permethrin Residues On Snap Beans
2127407	Permethrin Residues In Asparagus
2127408	Permethrin Residues In Soybean Process Fractions
2127410	Permethrin Residues On Field Corn
2127411	Permethrin Residues On Potatoes
2127412	Permethrin Residues On Sunflower Seeds And Stover After Aerial Applications
2127413	Permethrin Residues On Mushrooms
2127414	Permethrin And Permethrin Metabolite Residues On Corn Fodder
2127415	Permethrin And Permethrin Metabolite Residues In Field Corn Process Fractions
2127416	Permethrin And Permethrin Metabolites On Potatoes
2127417	Permethrin Residues In Tissues And Eggs After Commercial-Type Applications To Chickens
2127418	Permethrin Metabolite Residues On Field Corn
2127419	Permethrin And Permethrin Metabolite Residues On Field Corn
2127420	Permethrin And Permethrin Metabolite Residues On Tomato Process Fractions
2127421	Permethrin Residues On Tomatoes From Aerial Applications
2127422	Permethrin And Permethrin Metabolite Residues On Horseradish Roots
2127423	Permethrin And Permethrin Metabolite Residues On Cabbage
2127425	Permethrin Metabolite Residues On Untrimmed Lettuce
2127426	Permethrin And Permethrin Metabolite Residues On Brussels Sprouts
2127427	Permethrin Residues On Citrus Fruit
2127428	Permethrin And Permethrin Metabolite Residues On Cauliflower
2127429	Permethrin And Permethrin Metabolite Residues On Cauliflower-Amendment
2127430	Permethrin Metabolite Residues On Apples
2127431	Permethrin And Permethrin Metabolite Residues On Broccoli
2127432	Permethrin Residues On Wheat
2127433	Permethrin Residues On Field Peas

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2127434	Permethrin Residues On Corn Fodder
2127435	Permethrin Residues On Grain Sorghum
2127436	Permethrin Residues On Pumpkins
2127437	Permethrin Residues On Asparagus
2127438	Permethrin Residues On Citrus Fruit
2127439	Permethrin And Permethrin Metabolite Residues On Sunflower Seed Processing Fractions
2127440	Permethrin And Permethrin Metabolite Residues On Peaches
2127441	Permethrin And Permethrin Metabolite Residues On Peanuts And Peanut Process Fractions
2127442	Permethrin Metabolite Residues On Pumpkins
2127443	Permethrin And Permethrin Metabolite Residues On Eggplant
2127444	Permethrin And Permethrin Metabolite Residues On Snap Beans
2127445	Permethrin Metabolite Residues On Grain Sorghum (Includes Raw Data)
2127446	Permethrin Metabolite Residues On Asparagus
2127447	Permethrin And Permethrin Metabolite Residues On Watercress
2127448	Permethrin Metabolite Residues On Citrus Fruit
2127449	Permethrin And Permethrin Metabolite Residues On Dry Beans
2127450	Permethrin Residues On Pistachio Nut Meats
2127451	Permethrin And Permethrin Metabolite Residues On Artichoke Buds
2127452	Permethrin And Permethrin Metabolite Residues On Pumpkins
2127453	Permethrin Residues On Snap Beans
2127454	Permethrin Metabolite Residues In Snap Beans
2127455	Permethrin Residues On Dry Beans
2127458	Permethrin Metabolite Residues On Collards, Kale And Mustard Greens
2127459	Permethrin And Permethrin Metabolites In The Processing Fractions Of Tomatoes
2127460	Permethrin Residues In Apples, Senaca Castle, New York - 1976
2127461	Permethrin Metabolite Residues On Dry Beans
2127462	Residues On Cottonseed From Permethrin-Chlordimeform And Permethrin-Methomyl Tank Mix Applications
2127468	Residues Of Permethrin And 3 Phenoxybenzyl Alcohol In Tissues From Ectiban Treated Swine (Trial No. 35NC79 002)

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2127470	Permethrin Residues On Cottonseed From ULV Applications
2127471	Permethrin And Permethrin Metabolite Residues In Cow Tissues
2127473	Residues Of Permethrin And 3 Phenoxybenzyl Alcohol In Tissues And Eggs From Ectiban Treated Chickens (Trial No. 35NC79 003)
2127474	Ectiban Insecticide: Residue Monitoring Under Section 18 Program For Fly Control In Caged Layer Poultry Houses 1979
2127475	Permethrin Residues In Lettuce, Ithaca, New York, 1975
2127476	Phase 3 Reformat Of MRID#S 35517-18 And 94609-10: Permethrin: Magnitude Of Residues In Or On Horseradish
2127477	Phase 3 Summary Of MRID # 151251, Permethrin: Magnitude Of The Residue In Or On Cantaloupe
2127478	Phase 3 Summary Of MRID 40446401 And Related MRID 40446402: Permethrin (Pounce) Insecticide-Determination Of Permethrin, DCVA And MPBA Residues In/On Asparagus
2127480	Phase 3 Summary Of MRIDS 133293 And 41065805. Ambush And Pounce Magnitude Of The Residue Pistachios
2127482	Permethrin: Residues In Tomatoes And Almonds
2127483	Permethrin: Residues In Lettuce
2127485	Permethrin: Residues In Walnuts, Addenda To MRID Number 072833
2127486	Permethrin (ICIA0557): Residue Processing Study Following The Application Of Ambush To Potatoes
2127487	Permethrin (ICIA0557): Residue Processing Study For Ambush On Apples
2127488	Magnitude Of The Residues Of Permethrin, Dichlorovinyl Acid And Meta-Phenoxybenzyl Alcohol In/On Spinach Treated With Ten Applications Of Pounce 3.2EC Insecticide Or Pounce 25WP Insecticide At 0.2 Lb Active Ingredient Per Acre Per Application
2127489	Permethrin (ICIA0557): Residue Levels In Alfalfa, Forage, Hay And Meal From Trials Carried Out In The USA During 1992
2127490	Magnitude Of The Residues Of Permethrin, Dichlorovinyl Acid And M-Phenoxybenzyl Alcohol In/On Field Corn Grain And Processed Product (Wet And Dry Mill Products) Treated With Pounce 3.2 EC Insecticide At Exaggerated Label Rates
2127491	Magnitude Of The Residues Of Permethrin, Dichlorovinyl Acid And M-Phenoxybenzyl Alcohol In/On Celery Treated With Ten Applications Of Pounce 3.2 EC Insecticide At 0.2 Lb Active Ingredient Per Acre Per Application
2127492	Magnitude Of The Residues Of Permethrin, Dichlorovinyl Acid And Meta-Phenoxybenzyl Alcohol In/On Field Corn Treated Using Pounce 3.2 EC Insecticide

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2127493	Magnitude Of The Residues Of Permethrin, Dichlorovinyl Acid And M-Phenoxybenzyl Alcohol In/On Sweet Corn Ears, Husks And Stalks Treated With Pounce 1.5 G And 3.2 EC Insecticides
2127494	Magnitude Of The Residues Of Permethrin, Dichlorovinyl Acid And M-Phenoxybenzyl Alcohol In/On Spinach Treated With Five Applications Of Pounce 3.2 EC Insecticide At 0.2 Lb Active Ingredient Per Acre Per Application
2127495	Magnitude Of The Residues Of Permethrin, Dichlorovinyl Acid And Meta-Phenoxybenzyl Alcohol In/On Field Corn Treated With Pounce 1.5 G And/Or 3.2 EC Insecticide
2127496	Magnitude Of The Residue Of Permethrin, Dichlorovinyl Acid And Meta-Phenoxybenzyl Alcohol Residues In/On Soybean Seeds(Dry) And Processed Products Treated With Ounce 3.2 EC Insecticide At A 60 Day PHI
2127498	Analytical Methods For The Determination Of Permethrin, Dichlorovinyl Acid And M-Phenoxybenzyl Alcohol Residues In/On Soybeans And Its Processed Products
2127499	Permethrin (ICIA0557): Magnitude Of The Residue Study On Alfalfa Seed And Seed Screenings After Treatment Of Alfalfa With Ambush Or Ambush 25W From Trials Carried Out In The USA During 1992
2127500	Permethrin (ICIA0557): Magnitude Of The Residue Study On Peaches After Treatment With AMBUSH And AMBUSH 25W From Trials Carried Out In The USA During 1992
1153371	Ambush 500ec - Crop Residue Data:Refs -115 - 120
1153372	Ambush 500ec - Crop Residue Data:Refs- 105-114
1153374	Ambush 500ec - Crop Residue Data:Refs- 121-123
1153382	Ambush 25wp - Crop Residues - Plums - Refs. 18-19
1153383	Ambush 25wp - Crop Residues - Pears - Refs. 20-21
1153394	Ambush 25wp - Crop Residue Data - Plums
1153548	Permethrin Residues - Data On Corn
1156371	Permethrin: Submission Of An MRL For Spinach To Allow Importation Of Treated Crop From U.S.A. Submitted:06/17/94 (Ref21;Rr90-296b;Tmu0850/B;Tmu1319/B;Ran-0159;S-138-84-08)
1157511	Permethrin Residues On Mushrooms (Tmu0625/B)(Ambush)
1157512	Section 18 Emergency Exemption Pounce Mushroom Spray Mist (June 1980) - Draft Label Plus Determination Of Permethrin Residues In Mushrooms (Ambush)
1157514	Determination Of Permethrin Residues In Mushrooms (G138;G9714:125-137)(Ambush)

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1202335	Permethrin Residue On Mushrooms
1202336	Section 18 Emergency Exemption/Pounce Mushroom Spray Mix
1202337	Detection Of Permethrin Residue In Mushrooms.
1202338	Detection Of Permethrin Residue In Mushrooms
1233268	Ambush (Permethrin) - Magnitude Of The Residue Study On Processed Tomato Products (0557-89-Pr-01/Rr 90-020b)
1242713	Ambush 500ec - Residue Study (Wheat)
1245308	Ambush 500ec - Residues On Grapes
1245309	Ambush 500ec - Residues On Tomatoes
1245310	Ambush 500ec - Residues On Peanuts
2127501	Permethrin (Fmc 33297) 120 Day Indoor Crop Rotation Study
2127502	Confined Rotational Crop Study In The Greenhouse With 14C-Labelled Permethrin
2127504	Permethrin Residues In Tomato Process Fractions
2127505	Permethrin Residues In The Commercial Processing Fractions Of Apples, Wenatchee, Washington - 1976
2127506	Permethrin Residues In The Commercial Processing Fractions Of Apples, Geneva, New York - 1976
2127507	Permethrin And Permethrin Metabolite Residues In The Process Fractions Of Laboratory Fortified Field Corn
2127508	Permethrin: Metabolism And Residues In Goats
2127509	Permethrin: Incorporation Of Permethrin In The Diet Of Laying Hens

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1141789	Permethrin Residues On And In Cattle Exposed To A Lewis Cattle Oiler Charged With 0.5% Permethrin Solution (Ectiban-25)
1142505	Permethrin Residues In Milk From Cows Treated With 1% Permethrin Pour-On
1152938	Bovine Tissue Residue Depletion Of Permethrin Following Spray Applications To Animals & Their Premises
1152945	Appln Of The Aoac Multi-Residue Method To Determination Of Synthetic Pyrethroid Residues In Celery & Animal Products
1152946	Analysis Of Egg Yolk For Permethrin-28829-A
1152947	Analysis Of Egg Yolk For Permethrin-28829-B
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E. Information Considered in the Environmental Risk Assessment

List of Studies/Information Submitted by Registrant

PMRA document number	Reference
1131667	Sorption/Desorption Of ^{14}C-Permethrin On Soils. (Pc-0156;Sc900199;138e3290e1)(Dragnet Ft). DACO 8.2.4.1
1131669	Mobility Of FMC 33297 In Soil (M-3703)(Dragnet Ft). Daco 8.2.4.1
1131670	Permethrin: Mobility of permethrin and its degradation products in soil (Ar2716b;5b.1/3)(Dragnet Ft). DACO 8.2.4.1
1131671	Leaching characteristics of soil incorporated permethrin following aerobic aging. Final Report (39227;138e3190e1;Pc-0162)(Dragnet Ft). DACO 8.2.4.1
1131672	The metabolism of ^{14}C-permethrin in sandy loam soil under anaerobic conditions (Hrc/Isn 236/91107)(Dragnet Ft). DACO 8.2.3.1
1131673	The effect of application rate and soil moisture content on the rate of degradation of ^{14}C-permethrin in aerobic sandy loam soil (Hrc/Isn 247/91296)(Dragnet Ft). DACO 8.2.3.1
1131674	Permethrin degradation in soil and microbial cultures (Donald Kaufman) (edited by m.elliot p.147-161 vol.14)(dragnet ft). DACO 8.2.3.1
1131675	Degradation of ^{14}C-carbonyl-*cis*- and *trans*-permethrin in soil (no.6)(dragnet ft). DACO 8.2.3.1
1131677	Degradation of ^{14}C -cyclopropyl- and 14c-methylene-permethrin in soil (no.7)(dragnet ft). DACO 8.2.3.1
1131678	The effect of soil temperature on the degradation of ^{14}C -carbonyl-cis, *trans*-permethrin in soil (no.8) (dragnet ft). DACO 8.2.3.1
1131679	Permethrin: Laboratory studies of the degradation of the pesticide in soil (tmj 1287b;ifmc 76-18)(dragnet ft). DACO) 8.2.3.1
1131680	Permethrin: The degradation of the pesticide in soil under laboratory conditions. iii (5b.1/6;tmj 1512b)(dragnet ft). DACO 8.2.3.1
1131682	Degradation of ^{14}C -carbonyl *cis*- and *trans*-, and ^{14}C -methylene *cis*- permethrin in flooded soil (no.9)(dragnet ft). DACO 8.2.3.1
1131683	Permethrin: The degradation of the pesticide in flooded soils incubated under laboratory conditions (5b.1/7;tmj 1527b)(dragnet ft). DACO 8.2.3.1
1131684	Determination of dissipation rate of FMC 33297 residues in soil (w-0065)(dragnet ft). DACO 8.2.3.1

1131685	Dissipation of FMC 33297 residues in soil (w-0182)(dragnet ft). DACO 8.2.3.1
1131689	Dissipation of FMC 33297 residues in soils following multiple applications (w-0116)(dragnet ft). DACO 8.3.2.3
1131690	Pounce 3.2 EC insecticide-terrestrial field dissipation (p-2703;138e4191r1). DACO 8.3.2.3
1131692	Status report on synthetic pyrethroid (FMC 33297) in soil and in surface run-off from cotton plots (dragnet ft). DACO 8.3.3.3
1131693	Permethrin: Degradation in river sediment, river water and in flooded soils (rj0008a)(dragnet ft). DACO 8.3.3.3
1131720	Hydrolysis of FMC 33297 insecticide (phase i)(w-0103)(dragnet ft). DACO 8.2.1
1131731	Technical report hydrolysis of FMC 33297 (cgp-77-12;g144)(dragnet ft). DACO 8.2.1
1131732	Pyrethroid phototdecompostion: permethrin (by Holmstead, Casida, Ruzo & Fullmer). DACO 8.2.1
1233646	Permethrin residues in samples from a 1980 Alabama runoff study, tmu0540/b. DACO 8.3.2.3
1248488	Persistence of four pyrethroid insecticides in mineral soil, organic soil. DACO 8.2.3.1
1248501	Persistence of five pyrethroid insecticides in sterile & natural mineral & organic soil. DACO 8.2.3.1, 8.2.4.1
1248502	Movement of cypermethrin decamethrin, permethrin, & their degradation products in soil. DACO 8.2.4.1
1131726	Accumulation studies: Laboratory studies of pesticide accumulation in fish: ^{14}C-alcohol (phenyl) labelled permethrin in the blue gill sunfish (p-2262;138e5489e1-20(dragnet ft). DACO 9.5.5
1131727	Accumulation studies: Laboratory studies of pesticide accumulation in fish: acid (cyclopropyl)- ^{14}C labelled permethrin in the bluegill sunfish (p-2314;138e548e1-1)(dragnet ft). DACO 9.5.5
1131728	Uptake, depuration and bioconcentration of ^{14}C -permethrin by bluegill sunfish. final report (pc-0117;138e5489e1;37676)(dragent ft). DACO 9.5.5

Additional Information Considered

Published Information

Environmental Fate and Effects Assessment

PMRA document number	Reference
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2431489	European Union, 1998, Permethrin - Volume 3. Annex B.-8 : Environmental Fate and Behaviour, DACO: 12.5.8
2431490	California Environmental Protection Agency, 2003, Environmental Fate of Permethrin, DACO: 12.5.8
2431491	Skidmore, M., 1994. Influence of Application Methods on the Degradation of Permethrin in Laboratory, Soil Aerobic Metabolism Studies. Pesticide Science. 42: 101 - 107. DACO: 8.2.3.4.2
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